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LEGAL MEDICINE AND TOXICOLOGY

BY

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PREFACE

THE object of the present work is to present in one volume the more usual phases of Legal Medicine in a somewhat concise manner, in order that the busy practitioner may have access to the more important points involved in the cases with which he, ordinarily, comes in contact and upon which he may be called upon to inform himself before giving testimony in such cases; and, also, in order that the student may have such a presentation before him, so that he may be able to learn the rudiments of the science and may prepare himself for the different examinations for licensure. No attempt has been made to include in this work all the subjects with which Legal Medicine may be concerned, nor to insert discussions of all substances that may give, or have given, rise to poisoning, the selection of subjects being purely arbitrary and based on the ordinary need of both student and practitioner for such information.

In the preparation of this work, practically all the available books on Legal Medicine, both old and new, have been consulted and utilized, and material excerpted from these in many cases. Extensive use has been made, especially, of such well-known works as *Legal Medicine and Toxicology* by Peterson, Haines and Webster, and *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, in some cases extensive quotations being made therefrom, but there is hardly a published work on the subject from which some references have not been taken. The medical literature has been closely scanned and direct references made to the findings of recent workers so that the present book is believed to be thoroughly abreast of the times from the standpoint of inclusion of the more important investigations on the various subjects involved. Efforts have been made to give, in every case, proper credit for the subject-matter included, but it is, of course, possible that some omissions have occurred, in which case the writer wishes to acknowledge his indebtedness to those who have not received recognition, as well as to those whom he has directly quoted.

It may appear, on consulting the extent of Part II, as compared with Part I, that undues tress has been laid upon Toxicology in this work. This is not, in reality, the case, but is due to the fact that the writer has thought it advisable to go much more thoroughly into the methods of isolation and identification of the various poisons discussed than is the case in other single volume works on the subject. While it is true that most of the important toxicological cases are handled by experts in this line, yet it not infrequently happens that the practitioner may be called upon to give an opinion, at least a preliminary one, as to the presence of poisoning from a certain substance, and the student may require much detail as to methods of detection in his college work, so that the inclusion of the detailed chemical methods may prove valuable to both of these classes of workers, as well as to those who are more frequently involved in such cases.

The writer has, as a rule, used throughout the work, the metric system of weights and measures, and the Centigrade thermometer scale, believing that the present tendency to the wider employment of these systems should be encouraged. In giving the names of drugs and chemicals we have adopted the nomenclature and spelling of the United States Pharmacopoeia (tenth decennial revision, 1925), and have, almost universally, stated the properties of the drugs as found in this work, although, in some cases, the physical constants are inserted as given by the International Critical Tables. By such a system of treatment, the discussions are given the weight of established authority.

The writer wishes to extend his thanks to his friends and colleagues, who have given him invaluable aid and advice concerning the inclusion of some of the subject-matter. He wishes, especially, to acknowledge his great indebtedness to his publishers, W. B. Saunders Company, for their great interest, patience, and unfailing courtesy during the period of preparation.

RALPH W. WEBSTER.

25 E. WASHINGTON ST.,
CHICAGO, ILL.,
October, 1930.

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LEGAL MEDICINE AND TOXICOLOGY

INTRODUCTION

Legal Medicine, Medical Jurisprudence, or Forensic Medicine may be defined as that branch of jurisprudence which applies the knowledge of all departments of medicine, or its correlated sciences, to the solution of questions at law. "The subject is one which calls for information and investigation along widely divergent lines, in following which members of the legal and medical professions may seek the advice and counsel of one another, in which case each acts in his specific professional capacity. Among the questions arising at times in legal procedures are such as concern the causes of death, the identity of the living and the dead, the results of wounds and injuries of all kinds, life and accident insurance, mental incompetence from various causes, malingering, legitimacy, abortion and infanticide, impotence, sterility and unnatural offenses, marriage and divorce, malpractice, and the many points involved in relation to the science of toxicology."

Just as we have in the practice of medicine the so-called "general practitioner", who must study and treat all types of disease and conditions presented to him, so we have had, in times passed, in the field of Legal Medicine those who attempted to qualify as advisors of the court in the elucidation of problems of widely varying character. However, the advances in the field of scientific medicine have been so marked in recent years that no single mind is able to carry the details of all of the many branches. The questions presented for solution in courts of law are so intricate, oftentimes, that it is not to be expected that any but carefully trained pathologists, neurologists, alienists, surgeons, obstetricians, chemists and other specialists would be in a position to act as real judicial advisors. In many cases the aid of several experts must be invoked, as the questions involved may necessitate a comprehensive knowledge of different fields. Hence, the courts demand that only those especially qualified by experience and special study along definite lines shall be called upon to aid in the clearing up of problems presented for solution. Such witnesses or advisors are known as "expert witnesses" and are asked to testify as to their opinions or as to the facts based on their special examinations of the case, or as to the deductions to be made from the facts set before the court by other witnesses. However, it not infrequently happens that certain questions arising may be answered by any well-qualified practitioner, so that such an one, even though he may not have made any special study of the points involved, may be called upon by the court to present general and special facts to the court.

Ordinary and Expert Witnesses.—In presenting themselves as witnesses before the courts, medical practitioners may assume the rôle either of ordinary or expert witnesses. The usual procedure in calling a witness is for the court to issue a *subpoena*, which directs the person named in the summons to appear at a specified time in a specified court to offer his evidence in the cause in question. If it is desired that the witness bring any records bearing on the case, a special type of subpoena, called *subpoena duces tecum*, is issued. A subpoena is always served upon an ordinary witness and may or may not be issued in the case of the expert. Once served it must be obeyed unless later instructions are given to the witness by the court of jurisdiction.

As *ordinary witnesses* their testimony must be based entirely on the facts observed by them through their own special senses. They may introduce only those points which they themselves know as a result of their examination, observation or treatment of the case involved. They may offer no deductions beyond those which are matters of every-day knowledge and which are capable of substantiation by the jury itself. They may state nothing derived from hearsay evidence and must limit their testimony to that which they actually know as to the facts involved. In this testimony they may, in some states, refuse to answer certain questions involving confidential matters between themselves and their patients, taking advantage of the rule of "Privileged Communications", but, in other states, this rule does not apply so that they may be required to answer any questions put to them, however confidential it may be considered, unless the answer would tend to incriminate them as witnesses or might blacken the character of one about whom the question was asked.

As *expert witnesses* they testify either to the facts gained by themselves through their own examinations or investigations of the case and as to the deductions or conclusions which they draw from these facts or from the facts as introduced by other witnesses. In this connection they may be called upon to answer hypothetical questions based upon the evidence in the case. Expert witnesses are essentially judicial advisors of the court and are expected to elucidate, by their statements of facts and their deductions, the points at issue in the case. "Where conclusions depend upon facts whose evidential weight can only be determined by those familiar with a particular specialty, these conclusions must be given by experts in such specialty." From the nature of the service which experts render, they are entitled to special fees for their testimony, but it is always wise to arrange for these extra remunerations before going on the witness stand.

The question not infrequently arises as to whether a witness, called to testify as to the facts observed by him, that is called as an ordinary witness, may be asked to interpret his facts or draw conclusions from those or other facts, that is to act as an expert witness but without the extra remuneration usually accorded such witnesses. The practice of the courts on this point differs in different states and the practice of federal courts in some states varies from that of the state courts. It may be stated that, in some states, the expert, when asked to answer questions involving expert knowledge of the points at issue, may refuse to answer such questions unless the attorney wishes to qualify him as an expert witness and assure him of the extra remuneration to which he should be entitled under such circumstances. In other states, however, the ordinary witness may be asked questions involving expert knowledge and may be compelled by the court to answer them under penalty of contempt of court for refusal to do so. The grounds, upon which the right to extra compensation on the part of the expert witness have been sustained in those courts which grant this privilege to such witnesses, are (1) that the time of the expert witness is more valuable than that of the ordinary man, (2) that the skill and accumulated knowledge of the expert are his property and that property should not be taken without just compensation, and (3) that the knowledge and skill of the expert witness may be treated as "particular services". In regard to these points it is to be said that there appears to be considerable agreement that extra compensation of an expert witness can not properly rest upon loss of time as a basis for such remuneration. With reference to the second point mentioned above, that skill and knowledge of the expert are his personal property and he can not be deprived of such property without compensation, there is some divergence of opinion as to just exactly what is meant by "property" in this connection. While many authoritative works[1] favor the contention that the expert's knowledge is his property to dispose of as he wishes, certain court opinions differ widely as to the use of this property. Thus, in the case of Dixon *v.* People[2] in which the judgments of the Circuit and Appellate Courts were affirmed by the Supreme Court of Illinois, Justice Magruder stated "It is not exactly accurate to say, that the mere abstract knowledge, acquired in the study of a special employment, is of itself property. It is the right to apply that knowledge to the accomplishment of a particular result, which constitutes property . . . But when a physician is asked a hypothetical question, and is called upon to give his opinion upon the facts stated in the hypothetical question while he is testifying as a witness in court, he is not thereby required to practice his healing art. He is merely making a statement, not for the purpose of affecting a cure or relieving a patient, but for the purpose of enabling the court and the jury to understand correctly a case, which is before the court. There is no infringement here of a property right. It may be conceded, that in a certain sense, the knowledge of the physician, acquired by special study, is property, but the question here is, not so much whether certain knowledge is property, as whether the requirement, that he shall answer a hypothetical question, is a taking of his property. Where he is required to make an application of his knowledge to a particular case, so as to secure a particular result, such as, for instance, the curing of a disease, or the healing of a wound, then he would undoubtedly be entitled to compensation. A physician or surgeon cannot be punished for a contempt for refusing to make a *post mortem* examination, unless paid therefor, nor can he be required to prepare himself in advance for testifying in court by making an examination, or performing an operation, or resorting to a certain amount of study, without being paid therefor. But when he is required to answer a hypothetical question, which involves a special knowledge peculiar to his calling, he is merely required to do what every good citizen is required to do in behalf of the public good." As stated in another case[1], the law allows no excuse for withholding evidence, which is relevant to the matters in question before its tribunals, and is not protected from disclosure by some principle of legal policy. In connection with the point involved in this discussion, Rogers[2] states: "Whether they can be compelled to testify in such cases, when no other compensation has been tendered than the usual fees of ordinary witnesses testifying to ordinary facts, is a point upon which the cases are not in harmony. In this country the cases are nearly balanced, and the question must be regarded as still an open one, although the weight of authority rather inclines to the theory, that the expert may be required to answer the question without additional compensation."

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[1] See Wharton on *Evidence,* Phillips on *Evidence,* Rice on *Evidence,* Lawson on *Expert Evidence,* etc.

[2] 168 Ill. 179.

Concerning the third point mentioned above, namely that the knowledge and skill of the expert witness may be treated as "particular services", it is to be said that this rests upon the reasoning of the court in the case of Buchan *v.* State[3], the opinion being based upon a statement in the Indiana Bill of Rights to the effect that "no man's particular services shall be demanded without just compensation." This opinion is dissented from in the case of Dills *v.* State[4].

In Illinois the practice is such that the ordinary witness may be called upon to answer questions involving expert knowledge without compensation other than that of the ordinary witness. In a case decided by the Supreme Court of Illinois,[5] it was held that an attending physician subpoenaed as an ordinary witness could not limit his answers to statements of facts observed by him, but must in response to questions propounded by counsel give his opinion on matters arising out of such facts, without compensation other than that of an ordinary witness. In the case of Dixon *v.* People (cited above), the Supreme Court of Illinois held that a physician having no knowledge of the facts of the case may be summoned as a witness in either civil or a criminal case and required to give his opinion in response to hypothetical questions without any compensation except that due him as an ordinary witness. In the federal courts, however, the practice seems to be that a physician cannot be compelled to testify as an expert unless arrangements have been made to compensate him for his services. This ruling would seem to be the logical one, as the skill and experience of a physician are most certainly part of his individual property. It has, however, been ruled that the refusal to answer any question, which a witness may lawfully be required to answer, is a contempt of court, and, if the witness persists in his refusal, he may be punished therefor.[1]

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[1] *Ex-parte Dement,* 53 Ala. 389.

[2] *Expert Testimony,* 2nd ed., p. 424.

[3] 59 Ind. 1.

[4] 59 Ind. 15.

[5] Wright *v.* People, 112 Ill. 540.

In the matter of interpreting evidence, there are many sources of error which may creep into the testimony of the expert. We are all familiar with the fact that people differ as to their powers of observation. If two or more persons witness an event and are asked to describe what they saw and the sequence of things as they saw them, it is not unlikely that there may be almost as many different versions of the happening as there were persons witnessing it. In other words, certain facts are prominent with one individual, while different things assume more importance in the minds of others. This is due to the variation in the acuteness of the special senses of the different individuals.

Further, there may be abnormalities of some of these special sense organs, which make it impossible for certain persons accurately to interpret what they may see or hear, for instance. There is little difficulty in testifying as to facts which are generally known and accepted. But, in the critical balancing of evidence, which should be especially prominent in the testimony of the expert, much will depend upon the extent and limitations of his experience along the lines involved. The chief sources of error in evidence have been well summed up as follows: "They consist of (1) deliberate fraud, as in all species of quackery; (2) wilful perversion of facts by pseudoscientists; (3) objective errors through limitation and defect of the senses; (4) limited horizon through defective experience and education; (5) insufficiency of the imaginative faculty; (6) vitiation of evidence under influence of the emotions; (7) the innate tendency of the mind to completeness, to dramatic unity in unraveling a mystery."[2]

It is probable that most of those who enter upon the practice of medicine feel or hope that it will never be their lot to be called upon to assume the role of a witness in a court of law. However, the first case to which he may be called may involve the practitioner in an investigation requiring his appearance in court. Once called, he can not shift his responsibility or avoid rendering all the assistance in his power in the solution of the questions at issue. It has been well said that "While it is the prime aim and object of the physician and surgeon to cure, and to save life, the medical jurist has to deal with problems ahead of these efforts; for example, while his immediate duty in a given case of cut-throat is to save the life of his patient, it may be required of him to give an opinion whether, from the character of the wound and other facts, such wound was inflicted suicidally or homicidally, and, if the former, whether the person, at the time the wound was inflicted, was or was not of unsound mind." (Glaister). A medical man, called to act in such a capacity, must, therefore, realize the importance and gravity of his situation and must, whether he wishes or not, cultivate habits of rapid and accurate observation of all possible points which may have a later bearing on the solution of the many questions, which are sure to arise in the case. In this connection it may be pointed out that it is often the most insignificant points, from the standpoint of the practitioner, that may become of the most extreme importance when viewed by the medical jurist.

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[1] See Samuel *v*. People, 164 Ill. 379.

[2] Peterson, Haines and Webster, *Legal Medicine and Toxicology*, 1923, I, 21.

The medical man, who is summoned as a witness, should be guided by a few simple rules of conduct so that he may appear to the best advantage while on the witness stand. Such suggestions have been so well presented elsewhere that we quote them directly here.[1] (1) In all cases in which your opinion is asked, it is well to arrange with your client for a proper fee for an investigation of the case and for your opinion on the facts he may set before you, with the express understanding that you are not to undertake to be a witness should you not be wholly satisfied as to the merits of the case; (2) before going on the witness stand make yourself thoroughly familiar with all the facts upon which you are to testify; (3) after acquainting yourself with all the facts bearing upon the case and carefully considering the opinions you would deduce from them, it is well to refresh your memory by reference to the views held by standard writers in relation to the subject in hand; (4) have a conference, if possible, with the experts of the other side for the purpose of interchanging views: (5) refuse to give evidence as an expert if you have the least doubt as to the correctness of your opinion founded upon the facts adduced; (6) on the witness stand let your bearing be dignified and grave, remember that the conviction or acquittal of a human being may hang upon your testimony, and avoid, therefore, any flippancy of manner; (7) in testifying use plain and simple language, avoiding technical, medical and scientific terms wherever possible; (8) having all your facts and opinions systematically arranged beforehand in your mind, be explicit and definite as to these, and especially as to dates, distances, sizes, weights, and all other measurements; (9) remember that your answers to questions are taken down, recorded and often printed, and that evidence you give this day may be reinvestigated at a subsequent trial, and your opinion in this case brought before you in some other issue, so that you should clearly understand each question put to you, and answer it deliberately, carefully and coherently; (10) answer directly and simply the question which is asked, volunteering nothing beyond what is required to place the facts or opinions clearly before the court. You will sometimes be asked in cross-examination to answer a question by "yes" or "no" only, and, in case such monosyllabic replies are not misleading, you should answer in this way; but if, as is often the case, they give only a part of the truth, it is your duty to explain this fact to the court and request the privilege of modifying the "yes" or "no" so that it may entirely represent your views; (11) it is sometimes difficult for a witness to avoid the unconscious bias, which makes him involuntarily hesitate to answer a question, when he sees it may do harm to the side that employs him; but you are there "to tell the truth, the whole truth, and nothing but the truth", whether it is good or bad for one party or the other, and your straight, unbiased answer to every question of examiner and of cross-examiner will do much to dignify your testimony and to impress the jury with the sincerity and value of your statements; (12) the cross-examiner may attempt to irritate you by his manner or by the character of his questions. Be careful, honest, and take no offense; (13) if asked a question, the answer to which you do not feel certain of, do not hesitate to say so. It is the wisest witness that knows when to say "I do not know"; (14) you may be asked if the work of such and such a writer is an authority, and, upon assenting to this, quotations may be cited in opposition to the facts you may have given. Remember that in science facts themselves are the only authority and that a book simply represents an attempt to present these facts. Books, therefore, are not in themselves authorities. Verify quotations and diagrams before answering questions connected with them; (15) the law permits you to refresh your memory as to facts, dates, dimensions, etc., by reference to your *original* notes, but you may not read your notes to the court; (16) it is well methodically to separate in your mind the facts which you have to present from the opinions which you deduct from them or deduce from the evidence offered to you. Should you, in answer to a question, state that your opinion is based in part on knowledge obtained from certain books, as well as on your personal experience, you should remember that you may be cross-examined by extracts from the book mentioned by you. This is a perfectly legitimate procedure, so that you should know in advance what may be expected, should the attorney attempt to cast doubt upon your testimony by reference to the authority cited by you. In one case the Supreme Court of North Dakota, in affirming a decision of a lower court, stated[1], "It is proper to cross-examine an expert witness with reference to data which form in whole or in part the basis of an opinion expressed by him; and when a particular authority had been relied on by the witness, it is proper to test his knowledge and the accuracy of his deductions by drawing his attention during cross-examination to the expressions of that particular authority. This is not permitted for the purpose of using the selected extracts as evidence but to enable the jury to weigh better the testimony of the expert."

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[1] See *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, I, 23.

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[1] Chezik *v.* Minneapolis, St. P. & S. S. M. Ry. Co. (N. D.), 218 N. W. 217.

LEGAL PROCEDURE

No conviction or punishment for a crime is possible without a formal and accurate accusation, which must charge the particular offense for which the accused is tried and convicted and, further, must be made in the form required by law. The special forms of accusation usually recognized by law, which are of importance to the medicolegal expert, are (1) Coroner's inquest; (2) indictment or presentment by a grand jury; (3) information by the public prosecutor; and (4) complaint or affidavit by a private individual.

1. Coroner's Inquest.—In our large cities, especially, and even in the most remote rural communities, there are many cases arising, which make it necessary that some one be legally authorized to inquire into the cause of death in those cases in which there may be reason to doubt that death was the result of natural causes. In most communities at the present time such officials are known as coroners, although in some counties of New York State (New York, the Bronx, Kings, Queens, Richmond, Erie, and Westchester), Essex county, New Jersey, and in the New England States, with exception of Connecticut, this office has been abolished in favor of that of medical examiner. In cases of death under ordinary circumstances the physician in charge of the case certifies as to the cause of death by signing the death certificate. Where death has been due, however, or is suspected of being due, to violent or unnatural causes, or death is sudden from casualty or unknown causes, or there may be reason to suspect foul play, the case automatically becomes one for investigation by the coroner, as the cause of death can not be certified by the attendant physician, who should refuse to sign the death certificate. The coroner has no jurisdiction in cases of disease unless he has reasonable grounds to suspect that the disease causing death resulted from violence or undue means. In cases of death without medical attendance both the Local Registrar and Coroner (in Illinois) are notified, and should there be no suspicion of violence, casualty or undue means, the local registrar may sign the certificate of death.

The power of the coroner is a judicial one, relating to inquiries into the cause of death by a jury of inquest over the body of the person, who may have come to his death under the above-mentioned conditions. The coroner acts in person, or, where there is a statute permitting it, may delegate his authority to a deputy. The coroner's jury consists of a variable number of men or women summoned by the coroner and sworn by him. This jury must investigate the circumstances and determine the cause of death, viewing the body and determining its identity if possible. While the law demands that the inquest be held only upon viewing the body (*super visum corporis*), this view may be made by the so-called coroner's physicians instead of the jury under certain conditions.

An autopsy is an essential part of the coroner's investigation in most cases, as by it the exact cause of death may, possibly, be determined. If the jury is to view the body, the autopsy should preferably not be made until after this part of the procedure; the jury, however, should not be present while the autopsy is being performed. If no sufficient cause of death is revealed by the autopsy, the coroner may order a toxicologic or other scientific examination of the organs, holding his further inquiry until the report of such investigations is available. The coroner summons as a witness before his jury any person, who may have knowledge as to the death in question. The proceedings are not directed against any special person, the function of this jury being largely concerned with the determination of the cause of death of the individual. Hearsay evidence is permissable at the inquest. The coroner and jury have the right to question the witness, although counsel for a suspected individual may do so with the consent of the coroner. Occasionally, the evidence introduced may lead to the discovery or suspecting of an individual as accountable for the death. In such contingencies, the coroner may commit the suspect to prison pending further legal investigation. After the evidence has been heard, the coroner instructs his jury as to the law and directs it to retire to consider its verdict. This verdict is reduced to writing and is signed both by the coroner and by the members of the jury. The suspected individual, if such there be, can not, however, be brought to trial on a coroner's verdict, a further legal step being necessary.

Such investigations of the coroner afford no certainty of the detection of crime, and, further, the system gives no protection to those who may be wrongly charged with crime, often screening a true criminal by a verdict based upon an imperfect and not well-directed inquiry. For these reasons, the office of coroner has been abolished, as stated above, in some localities and will, probably, be more or less generally eliminated in the near future. "A thorough and searching investigation into the cause of death is perhaps one of the most important and in fact indispensable functions of a community. The scientific determination of the cause of violent deaths is beyond the power of the old-fashioned coroner. Science will aid justice, if given a chance."[1] In place of the coroner, the medical examiner takes over the functions above mentioned in the states previously cited. These examiners, who are appointed by the governor, investigate the cause and manner of death of persons who are supposed to have come to their death by violence, by a casualty, by suicide, or suddenly when in apparent health, or when unattended by a physician, or in prison, or in any suspicious or unusual manner. These medical examiners can not, of their own motion, hold an inquest over a dead body, except in New York, where the procedure is somewhat different. On notification by the medical examiner that an inquest is necessary, a justice of the police, district, or municipal courts or trial justices having jurisdiction over the place in which the body is found may hold the inquest. The law requires that an inquest be held where death arises from the act or negligence of another or from the operation of a railroad, street railway, or motor vehicle, but leaves to the discretion of the medical examiner the calling of inquests in other cases, although the attorney general or district attorney may call an inquest following death from any casualty. The autopsy is held by the examiner only when authorized by the district attorney, mayor, or selectmen of the district, city, or town in which the body lies. The examiner is then empowered to employ competent individuals to perform scientific investigations, reports of which are embodied in the official report of the examiner. In New York City, as mentioned above, the chief medical examiner, who is appointed by the mayor, has supreme power of decision in regard to the performance of his duty. Autopsies are performed by him, or his assistants, whenever, in their opinion, the cause of death is not ascertainable on examination and from the history of the case. The functions of this office are purely investigatory, the medical phases being separated from the legal phases of the work. This system of medical examiner seems to make for simplicity, utility, and efficiency, so that it might be adopted in general over the old and inadequate coroner system. As Leary[1] remarks: "The coroner in this civilization is an anachronism. A necessary element in the primitive police systems of early Anglo-Saxon and colonial governments, he has no place in modern governments. His duties require him to be an expert in both medicine and law. The duty of determining whether the death of a human being was due to criminal violence or not is a purely medical function; the decision as to who caused the death is a legal or judicial function. The coroner system is a remnant of past and obsolete usages, and is wholly unsuited to the needs of the present time."

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[1] Gettler, "Why the Coroner System Has Broken Down", National Municipal Review, 1924, **13**, 560.

2. Indictment or Presentment by Grand Jury.—An *indictment* is a written accusation of a crime drawn up by the public prosecutor and submitted to the grand jury and by them found and presented upon oath or affirmation as a true bill. Should the coroner's jury or the medical examiner find that the probability exists that a crime has been committed, the verdict of the jury or examiner is referred to the state's or district attorney, who draws up a bill of indictment, which sets forth the nature of the crime and the name of the suspected person. This bill is submitted to a special body of persons, called a grand jury, consisting of not less than 12 nor more than 23 members, whose duty it is to ascertain whether there is sufficient ground of suspicion of the accused person to justify a trial by petty jury. The jury deliberates in secret, calling such witnesses as may throw light on the case, and paying special attention to the evidence as given by the scientific experts. If the jury decides that the evidence justifies a trial in open court, the indictment is returned to the prosecuting attorney marked "true bill"; but, if the evidence is not so regarded, the bill is ignored. A true bill leads to a trial, but this fact does not presuppose the indicted person to be guilty.

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[1] Jour. Amer. Med. Assoc., 1927, **89**, 579. See, also, Schultz and Morgan, Bull. 64, National Research Council, 1928; Editorial, Jour. Amer. Med. Assoc., 1929, **92**, 2024; 1929, **93**, 196; 1929; **93**; 1067.

A *presentment* is the notice taken by the grand jury of an offense from its own knowledge or observation, or of its own motion on information from others, without any bill of indictment having been submitted by the public prosecutor. This presentment, when offered, later becomes merged in an indictment, which is drawn up, the latter then becoming the real basis of the prosecution. At common law an indictment will lie for all treasons, felonies, and misdemeanors, and, also, for any offense created by statute, unless the statute points out some other mode of prosecution. In some jurisdictions a presentment is given the same force as an indictment, so that the accused may be arraigned and tried thereon, without any indictment being preferred and found.

3. Information.—An *information* is a written accusation of crime preferred by the public prosecutor without the intervention of the grand jury. The prosecutor may act on information which he himself has, that a crime has been committed, or on information which he obtains from one or more reputable citizens. At common law an information will lie for any misdemeanor, but not for a felony, but in some jurisdictions there are constitutional provisions, which prevent prosecutions by information for capital or otherwise infamous crimes, or for felonies, or for crimes subject to certain punishment, and, in some states, there are provisions preventing prosecution by information for any crime, except petty offenses cognizable by justices of the peace or police magistrates.

4. Complaint or Affidavit.—A *complaint* or *affidavit* is a written accusation of crime made by a private individual, or by an officer other than the public prosecutor. In the absence of statutory requirements to the contrary, a complaint may be made by any person, who legally can be a witness and who has knowledge or information of any violation of the criminal law. The filing of the affidavit, naming the offense and the person charged with its commission, is the first step in giving the magistrate jurisdiction over the person so charged. If the magistrate is satisfied that there are good grounds for believing the charge, he may issue a warrant of arrest. After the issuance of this warrant and after the appearance of the accused before him, the magistrate may proceed to hold a "preliminary examination", which is not a trial as the only issue involved is the question of the establishment of a prima facie case. If the magistrate feels that the charge is reasonably established, he may bind the accused over to appear at a certain term of a particular court to answer to the charge or may, in his discretion, commit him to jail.

The Trial.—The actual trial of the accused is conducted in open court, following the accusation in the forms mentioned, before a judge and a petty jury composed of twelve members. After the selection of this jury, it is sworn in by the judge, the indictment is read, and the accused is required to plead "guilty" or "not guilty" to the charge. To this trial the witnesses, medical and lay, are summoned by subpoenas which must be obeyed. It is here that the witness will be subjected to a severe and grilling examination and should follow closely the rules previously outlined. After the evidence is introduced and the attorneys for prosecution and defense have presented their closing arguments, the jury is instructed by the judge and then retires to deliberate upon its verdict. The finding of the jury settles the fate of the accused and substantiates or disproves the verdict of the coroner's jury and the indictment of the grand jury. For certain reasons, however, a new trial may be granted or an appeal may be taken to a court of higher jurisdiction.

PART I
LEGAL MEDICINE

CHAPTER I

LEGAL RIGHTS AND OBLIGATIONS OF PHYSICIANS

THE RIGHT TO PRACTICE MEDICINE

Although originally a common law right, in which the administration of aid or medicine or the performance of surgical operations was free to anyone who thought himself competent, yet the importance of regulating such practice became gradually apparent, so that laws, varying from time to time, were enacted covering the practice of medicine. The necessity of regulating by law such an intricate and delicate art as the practice of medicine is generally conceded, but it was not until about the middle of the nineteenth century that state licensure was universally adopted in this country. Such laws are enacted under the "police power" of the state to protect the health of the community and their validity has been generally maintained by the courts. The laws of the various states differ considerably in their requirements for the practice of medicine and almost none of them are to be regarded as satisfactory.[1] At the present time no one has the right to practice medicine without having the necessary qualifications of learning and skill and the statutes require that those, who profess to have such qualifications, shall show evidence of them in the form of a license from a body designated by the state as competent to pass on them. While the statutes of the various states vary in their exact terms, most of them direct that one shall obtain a license to practice medicine from the proper licensing board of the state in which he is to practice and that this license shall be contingent upon the completion of a course of prescribed study in a recognized medical school and, also, upon the passing of an adequate examination held under the direction of the licensing board. Some of the states, but by no means all of them, permit the issuance of licenses by reciprocity with certain other states. After the issuance of the license, it must be registered by the holder with the Clerk of the County in which the physician desires to enter upon his practice. Obviously, the Board issuing the license has the power of revocation for unprofessional conduct or for just cause.

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[1] See Kelly, "Regulation of Physicians by Law", Amer. Med. Assoc. Bull., 1924, **19**, 181; Tobey, "Medical Practice and the United States Supreme Court", Jour. Amer. Med. Assoc., 1927, **88**, 347.

The meaning of the term "practicing medicine" is defined somewhat differently by the statutes of the various states, but the following may be taken as generally acceptable: "Any person shall be regarded as practicing medicine or treating human ailments, who shall treat or profess to treat, operate on or prescribe for any physical ailment or any physical injury or deformity of another." It is not necessary that a person actually use drugs to be regarded as practicing medicine.[1] Most of the states have exemption clauses in the acts regulating the practice of medicine, which exclude certain methods of treatment from being classed under the heading of the true practice of medicine. Thus, this exemption is covered by the following statements in Section 37 of the Illinois Medical Practice Act of 1923: "This Act shall not apply to dentists, pharmacists, optometrists, or other persons lawfully carrying on their particular profession or business under any valid existing Act of this State regulatory thereof, nor to persons rendering gratuitous services in cases of emergency, nor to persons treating human ailments by prayer or spiritual means as an exercise or enjoyment or religious freedom." It happens, in consequence of such regulations, that many different systems of practice thrive in the various states. However, the courts do not recognize any system or school of practice as better than another, questions of malpractice being decided purely on the usage in the particular school of medicine to which the practitioner belongs.

CONTRACTURAL RELATIONS BETWEEN PHYSICIAN AND PATIENT

Having obtained this license to practice and properly registered it in the county of his practice, the physician is ready to incur his obligations and to receive the benefits due him from the community. The duties and obligations of physicians and patients grow out of their reciprocal contractual relations. These contracts may be either expressed or implied, the former being rare and usually in writing and including any stipulation not contrary to public policy. The implied contract between them, which is the usual form of contract, is in force whenever the physician accepts a call or begins his treatment of a patient.

The services of the physician are purely voluntary, that is he has full liberty to choose those cases which he will treat and to reject those which he does not care to handle. He is in no way legally bound to comply with requests for his services, although he would probably hesitate to refuse aid in an emergency. However, once having undertaken a case, he is not at liberty to discontinue attendance upon it, without reasonable and proper notice has been given the patient of the intention of leaving the case and time is allowed to obtain an acceptable substitute. Should one physician recommend another as his substitute, the former is not liable for the acts of the latter providing the patient accepts the substitute and he is one in independent practice and of ordinary skill and ability. It should be mentioned that the obligation of the physician to remain on the case is in marked contrast to the right of the patient to dismiss the physician at any time, unless there are express provisions for a certain period of treatment. In his relationship with his patient, the attending physician should not introduce into the sick-room any stranger (other than a physician) without the consent of the patient, as this would destroy the confidential character of the association.

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[1] See State *v.* Hughey (Iowa) 226, N. W. 371.

Having undertaken a case, the physician by implied contract with his patient is bound not only to possess ordinary and reasonable skill but, also, to use due care and diligence in the exercise of this skill. He does not contract for extraordinary or unusual skill, but simply for the average, reasonable and ordinary skill possessed by those practicing in the same or similar localities and following the same school of practice. The physician contracts to use his best judgment in the treatment of the case, but he is not responsible for errors in judgment providing the methods followed are such as are generally employed by his system of practice and providing that his judgment is based on an intelligent appreciation of the case in hand.[1]

In this connection it is well to point out that the physician is held to strict accountability for failure to use every diagnostic means in his power to insure a proper diagnosis and, hence, a scientific treatment of the case in hand. Courts have constantly stressed the importance of diagnosis. Thus the Supreme Court of Alabama[2] states: "In other words, after a diagnosis of the disease of the patient, he applies the remedy most suitable to its cure." And the Supreme Court of Idaho[3] asserts that "This court concludes that the trial court was justified in finding that the physician's failure to use modern methods of diagnosis could not be considered reasonable treatment within the meaning of the statute. The same was true of the treatment given after the diagnosis."

Further, as part of his duty to his patient, the physician must instruct both patient and attendants in regard to the handling of the case, giving them instructions, for instance concerning the time of giving and the dosage of all medicines, what diet to adopt, what type of baths to employ, what attention is necessary for the bowels and other eliminatory organs, what care should be given to injured parts, etc. All of the above contracts are implied whether the patient is expected to pay for the treatment or whether he be of the so-called charity type.

On his part the patient contracts to give the physician full and complete information concerning his case and his antecedent and family history; to follow out the instructions given him by the physician; and to remunerate the physician for his services. In obtaining information concerning the history of the case or in his daily contact with his patient, highly confidential matters may be revealed by the patient, which

[1] See DuBois *v.* Decker, 130 N. Y. 325.

[2] Bragg *v.* Alabama, 134 Alab. 165.

[3] Johnston *v.* A. C. White Lumber Company, Idaho, 217 Pac. R. 979.

subjects the physician regards as "Privileged Communications" and will hold inviolate (see later discussion of this subject).

The obligation to pay for such reasonable and just fees as prevail at the time and place for the services rendered by the physician devolves upon the one receiving the services, that is upon the patient. This is true if he be the financially and legally responsible member of the family. If, however, the patient be the wife or a minor child, then the head of the family becomes the party responsible for the payment of the fees. If the father be dead, then the mother of the minor child would be liable, unless the child has a separate estate. These obligations hold even though the child is not living with his parents, unless the separation is so complete as to release the parent from the liability. If the child be of age, then the parent is not liable unless he asks that the services be rendered or wishes to assume the responsibility.[1] Further, the person summoning the physician to attend a patient does not contract to pay for the services unless he is so related to the patient that he is legally obligated to pay. The reason for this ruling is clear, as the party calling the physician may have been simply a messenger and in no way connected with the family or the patient receiving the services, so that he incurs no liability by acting for the legally responsible parties. The fact that the patient is not cured or even benefited by the treatment instituted is no bar to recovery of fees, as there is nothing in the implied contract between physician and patient that implies or guarantees a cure.

The patient, or the responsible member of the family, is, likewise, responsible for the fees of the consultant, even though the consultant be summoned by the attending physician. If the patient accepts the services of the consultant, the law assumes that he is responsible for the payment of the fees. The estates of deceased individuals are liable for the physician's fees. Also, the estates of insane persons are liable for the medical treatment of the individual, but no contract for a definite fee may be made with those of unsound mind.

There has been considerable misunderstanding concerning the obligations of so-called "third parties" in relation to the payment of the fees of the physician. A master is not bound to pay for medical services rendered a servant, unless he expressly agrees so to do. A much mooted question is the liability of a corporation for services rendered to a party in case of accident or injury for which the corporation is responsible. It is now generally accepted that an agent may bind the company for emergency services, but that any later attendance upon the case must be approved by one having authority to act for the corporation in financial matters. If the injured person, himself, summons a physician other than the one connected with the responsible corporation, he alone is responsible for the payment of the fees, unless he has been given the privilege of calling his own physician by a responsible officer of the corporation. Where a corporation maintains a regular physician and his services are offered to an injured party and are refused, then the corporation can not be held for other medical attendance called by others, unless such corporation expressly consents to such a procedure through a responsible officer. Under the Workmen's Compensation Laws, which are based on the theory that losses due to injuries to employees arising out of any industry are proper charges against the cost of operating such industry, physicians are assured of a certain definite fee, which may, in some cases, be subject to review by the workmen's compensation board, unless there is an express agreement between physician and corporation as to the fees to be allowed. There is, however, nothing in such laws that limits the right of an employee to contract for better services or for longer services than those provided for in the acts and to pay the difference in fees himself. If a physician continues his treatment of an injured employee longer than the time allowed in these laws and has no understanding with his patient as to payment of fees beyond those for which the responsible corporation is legally bound under the terms of the compensation acts, the physician must look to the patient for payment of the excess fees or charge them to charity.[1] As to the legal responsibility of the corporation and of the physician employed by the corporation for damages arising in the course of treatment the courts have ruled that the relation of master to servant, in which the rule of *respondeat superior* (let the master answer) applies, does not exist between a railroad company (for instance) as employer and a surgeon employed to treat an injured employee, the reason being that the employer has no right to control the surgeon in the treatment of the case. Where an employer, under the Workmen's Compensation Laws, withholds from the wages of its employees a small monthly amount, with the aggregate of which it employs physicians and surgeons to treat such as become ill or injured, and in doing so it is not promoting its own interest by making a profit out of such employment, such employer is not liable to an injured employee for the carelessness or malpractice of such physicians or surgeons in charge of the case, provided it has used reasonable care in its selection of such physicians and surgeons. However, if the injured employee should be refused surgical attention and hospital treatment by his employer, it is his duty to secure such treatment elsewhere and to hold his employer responsible for the cost thereof.[2]

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[1] See Bailey *v.* Yowell (Mo.) 266 S. W. R. 324.

PRIVILEGED COMMUNICATIONS

In the course of his relations with his patients, a physician not infrequently receives private and confidential communications regarding matters which may or may not be pertinent to the treatment of the case in hand. Such communications or information may, however, become very important in the judicial investigations to which the physician may be summoned. These private or confidential communications are known as "Privileged Communications", although the common law concedes no special privilege of this sort to the physician. According to the common law, no medical man may claim exemption from answering a question because the answer might involve a violation of secrecy or might implicate the character of a patient, although he may refuse to answer it if, in so doing, he incriminates himself. In some of the states such a communication is excluded from introduction into evidence "because greater mischiefs would probably result from requiring or permitting its admission than from wholly rejecting it." In New York, for instance, "A person duly authorized to practice physic or surgery shall not be allowed to disclose any information which he acquired in attending a patient in a professional capacity, and which was necessary to enable him to act in that capacity." Such provisions as the above are found in the statutes of many states, but in many of the other states there are no statutes restricting the nature of the disclosures, which a physician may be compelled to make in a court of law. Whenever a communication, however, is made in the presence of a third person, it is not a privileged communication within the purview of the statutes.[1] It must be remembered that the relation of physician and patient exists in a hospital just as well as in private practice, so that reports from hospital records have been declared to be in contravention of the statute of privileged communication and can not be introduced in evidence in those states where such rules are in force.[2]

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[1] See Woodward, "The State Associations and the Workmen's Compensation Laws", Bull. Amer. Med. Assoc., 1925, XX, 22 and 43; also, Kessler, "The Physician and Workmen's Compensation," Jour. Amer. Med. Assoc., 1928, **90**, 825.

[2] See Borgeas *v.* Oregon Short Line R. Co. et al. (Mont.) 236 Pac. R. 1069.

The protection afforded by this rule is more in the interest of the patient than of the physician. The rule is qualified in some states by the exception that the privilege may be waived by the patient, by the executors, surviving husband or widow, or by any heir at law or next of kin. The witness must know the law of the state in which he is testifying, before he claims the protection that his information is of a privileged character. It is, however, undoubtedly true that the honorable physician will not reveal the confidence of his patient, unless a waiver of the privilege be made, and that he will always preserve inviolate every secret and confidence obtained in the course of his professional duties. In acting in this manner and in refusing to answer questions involving what he believes to be a matter between himself and his patient, the medical witness must remember that he may be punished for contempt of court for such refusal, but he will rest assured that he has merited the confidence of his patient and has lived up to the higest ethics of his profession.

This question of the confidential nature of information obtained by a physician from his patient may, not infrequently, become of importance outside of courts of law. Very delicate situations arise in the practice of medicine, when it may become necessary to reveal the existence of infectious disease to other parties. This question and the action to be taken has been well outlined in the Principles of Medical Ethics of the American Medical Association as follows: "There are occasions, however, when a physician must determine whether or not his duty to society requires him to take definite action to protect a healthy individual from becoming infected, because the physician has knowledge, obtained through the confidence entrusted to him as a physician, of a communicable disease to which the healthy individual is about to be exposed. In such a case, the physician should act as he would desire another to act toward one of his own family under like circumstances. Before he determines his course, the physician should know the civil law of his commonwealth concerning privileged communications."

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[1] State *v.* Knight (Iowa), 216 N. W. R. 104.

[2] Metropolitan Life Ins. Co. *v.* McSwain (Miss.), 115 So. 555.

DYING DECLARATIONS

From the nature of his professional duties, it not infrequently happens that the attending physician comes into possession of facts that are unknown to others and which may prove of importance in solving the question of guilt of an accused or even of an already convicted party. Even before any suspicious circumstances have come to light, a physician may be summoned to a person who has been suddenly attacked or seized with a severe illness. Such a patient, believing himself about to die and that his recovery is impossible, may make to the physician statements as to the circumstances surrounding the infliction of a wound, the administration of a poison, or the particulars of a crime long since committed. Such statements are known as "Dying Declarations" and are received in evidence without being sworn to, providing they are the utterances of a same mind,[1] the law assuming that the person making the statement has in mind the conviction of impending death and that such a statement has the force of one taken under oath. In prosecutions other than for homicide or abortion, the dying declarations of the person injured are not admissable as such; and even in prosecutions for homicide, statements of the deceased made after receiving the fatal wound or poison may not be received either for or against the accused. In several states the dying declarations of a woman whose death resulted from an abortion or an attempt to procure an abortion have been made admissable by statute, but this is not the case in some states, as for instance in Arkansas[2] where there is no statute to this effect.

It is wise, if time permits, for the attending physician, to whom such statements are made, to summon one authorized to take depositions, but if, as often happens, affairs are critical, the physician may be forced to take down what is said. No attempt should be made by him to interpret the statements or to introduce words other than those actually used by the one making the statement. He should receive what is voluntarily uttered and question the patient only for the purpose of explaining ambiguous or contradictory statements. If possible, the person making the statement should sign the subject-matter written down by the physician and the fact should be stated that the patient believes himself about to die. It is the duty of the physician, in case the individual dies, to place these statements in the hands of the prosecuting attorney for his information in investigating the matter.

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[1] See Lipscomb *v.* State, 75 Miss. 559; 23 So. 210.

[2] See Winfrey *v.* State (Ark.) 296 S. W. R. 82.

THE MAKING OF WILLS

With respect to the average patient, the drafting of a will is a proper function of the lawyer. However, in the case of a patient *in extremis* a physician may be confronted with the necessity of drawing up a will or, what is, perhaps, more frequent, of witnessing one made at such a time. "It would be useful," says Blackstone, "if the medical attendant were acquainted with at least the formal part of executing wills: in the moment of danger and distress, when all around the bed of death are confused with fear or overwhelmed with affliction, the physician, probably a confidential friend, whose duty and habit insures self-possession, may be the only person competent to advise."

It is highly desirable that the physician have a general idea as to the requirements entering into the making of a valid last will and testament.[1] By far the largest number of will contests turn on questions of fact, such as whether or not there was undue influence and whether or not there was mental capacity on the part of the testator; and do not grow out of any alleged informality in the preparation or execution of the will.

A will is defined as a disposition of property to take effect on or after the death of the person making the will. The essential requirements are as follows: The testator or testatrix must be of sufficient age, that is, usually, 21 years for the male and 18 for the female; the instrument must be signed by the testator or by some other person by his request and direction, and it must be signed in the presence of the attesting witnesses (usually two) and they must affix their signatures in the presence of the testator and of one another; the will must be dated on the date of execution and must be read by or to the testator; the person named as executor in the will should not act as an attesting witness, nor should any person act as a witness, who may be a beneficiary or legatee under the will; the testator must not be under duress, must not be subject to undue influence, and must have sufficient mental capacity to understand the full nature of the instrument and its contents; he should understand in a general way the extent of his property and should realize his relationships to his various heirs; and he should inform the witnesses that it is his last will and testament and that he wishes them to sign as attesting witnesses.

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[1] See Fenning, "The Making of Wills by Persons *in extremis*", Jour. Amer. Med. Assoc., 1923, **80**, 1795.

The real difficulty, on the part of the medical attendant, will be the decision as to the question of whether or not the testator has what the law calls "testamentary capacity". The point involved here is whether or not the testator has the ability to make *a* will, not the ability to make a particular will. It is generally admitted that there are four points necessary to constitute mental or testamentary capacity. These are (1) An understanding of the fact that a will is being made; (2) testator must have sufficient memory to know the nature and general extent of his estate; (3) testator must know his heirs and those bound to him by ties of blood; and (4) he must be able to keep these facts in mind long enough to form a rational judgment in relation to the disposal of his property. In the making and execution of the average will, its terms are known only to the testator and the lawyer who drafts it. It is not required, nor is it usually the fact, that the witnesses have any knowledge as to the disposition of the estate as directed in the will. If the physician has any doubt as to the testamentary capacity of the individual, he may very properly decline to witness the document until he has read its contents. In determining testamentary capacity, the physician must make such a test as takes into consideration the normal mental condition and habits of the particular individual, who is about to make a will, and then determine to what extent the illness of this individual has influenced him in the making of the will and whether, in the making of the will, he has been subjected to any undue influence.

OBLIGATIONS OF THE PHYSICIAN TO THE STATE

In entering upon the practice of medicine, the physician assumes certain obligations not only toward his patient but, also, to the State. While he professes to have ordinary skill in the healing of disease and obligates himself to use due care and diligence in the exercise of this skill, and offers his license as assurance that he has the proper legal qualifications, he, further, holds himself out as one possessing such moral qualities as make him a fit person to enter into very confidential relations with the sick and binds himself to be a proper person to be permitted free and constant access to the home and private rooms of the sick. In his dealings with his patients, with his brother physicians, and with the public and State he should follow the Principles of Ethics as laid down by the American Medical Association, or by the recognized tenets of his particular school of practice.

In assuming such obligations, the physician is required by law to make certain reports to the State Department or Boards of Health as to many cases which he may treat, for the purpose of a check on the Vital Statistics of the community as well as for the purpose of furnishing data which may prevent the spread of some of these diseases. Further, he is required to follow certain statutes concerning the prescribing and use of narcotics and of alcoholic beverages. It is in this relation of Physician to State that the practitioner is brought into close touch with the science of Legal Medicine, inasmuch as he must assume a watchfulness against unfounded criminal charges being made against the innocent and must, also, aid in the detection and punishment of crime.

Contagious Diseases.—Every physician must report to his local Board of Health every caes of contagious disease, of whatever type, that comes under his care. The list of these diseases is a long one and need not be given here. However, it is well for each physician to know thoroughly just what diseases he is required to report in his particular state, as some difference is found in the statutes, especially as regards venereal diseases. This duty, placed upon the physician by the State, is one that should be promptly and explicitly followed, as failure to report such diseases may delay the establishment of proper quarantine and result in rapid spread of the disease, so that it may become epidemic. It should be mentioned here that in making such reports the physician is not liable for a mistaken diagnosis, provided he has used his best judgment in the matter.

Considerable discussion has arisen over the question of the power of the State to make and enforce laws having to do with compulsory vaccination. In compiling a list of court decisions relative to vaccination, Tobey[1] states that "Vaccination requirements form a valid exercise by the state of its police power." Vaccination has, within reasonable limitations, been almost universally upheld by the courts as a proper exercise of this police power. A regulatory law must be a reasonable one, but to require that, during an epidemic or threatened epidemic of smallpox, all persons who had been exposed or reliably suspected of exposure should either submit to vaccination or be quarantined would be entirely reasonable and upheld by practically all courts. "With regard to the exclusion of unvaccinated children from school, there is some conflict in the decisions. The weight of authority, however, upholds as a valid exercise of the police power the requirement that children be vaccinated before attending schools, and their exclusion from school if they have not been so vaccinated." In cases of emergency, such as threatened epidemics, compulsory vaccination is upheld in practically every state.

Death Certificates.—Every physician must report to the Bureau of Vital Statistics of his state the cause of death of any of his patients. This death certificate is usually looked after either by the hospital authorities or by the undertaker, but must be filled out and signed by the physician, and, in most states, is necessary before a body may be buried. The details of this certificate will be given later in the Chapter dealing with Death in its Medicolegal Relations. It may, however, be stated here that if a physician is not certain as to the cause of death or if the death has been due to violence or to suspicious causes, he should refuse to sign the certificate no matter how much pressure is brought to bear by the surviving members of the family. In such cases the coroner automatically assumes charge of the case and investigates the cause of death.

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[1] "Vaccination and the Courts", Jour. Amer. Med. Assoc., 1924, **83**, 462.

Birth Certificates.—Likewise, physicians are obligated to report all births arising in their practice within 10 days of the birth. Unfortunately for statistics, many physicians are very lax in making such reports of births. It not infrequently happens that this failure on the part of the physician leads to considerable difficulty when an attempt is made, at some later period, to prove the question of legitimacy, of inheritance, etc. Such discussions will be taken up later.

Prescribing of Narcotics.—Every physician, who may wish to prescribe narcotics in his practice, must register with the collector of internal revenue of his district and receive, after payment of the requisite fee, authority, in the form of a registry number, permitting him to prescribe and dispense such remedies for a period of one year. The provisions of the federal law, known as the Harrison Law approved December 17, 1914, apply to the sale and dispensing of preparations of opium and coca. The law does not require official order blanks for the purchase or for the physician's private dispensing of preparations and remedies which do not contain more than two grains of opium, or more than ¼ grain of morphine, or more than ⅛ grain of heroine, or more than one grain of codeine, or any salt or derivative of any of them in one fluid ounce, or, if a solid or semi-solid preparation, in one avoidupois ounce; or to liniments, ointments, or other preparations which are prepared for external use only, except liniments, ointments, and other preparations which contain cocaine or any of its salts, or alpha or beta eucaine or any of its salts or any synthetic substitute for them: *Provided*, That such remedies and preparations are sold, distributed, given away, dispensed, or possessed as medicines and not for the purpose of evading the intentions and provisions of the Act. Each prescription, calling for narcotic preparations not exempted as above, must be in writing, must bear the signature, federal registration number and office address of the physician, must be dated, must bear the name and address of the person for whom prescribed, and must be preserved by the druggist for a period of two years, the copy being retained by the physician for the same period. Physicians, who dispense their own medicines, must keep for a period of two years a record of all such drugs so dispensed, except such as may be dispensed or distributed to a patient upon whom such physician shall personally attend, such record showing the date of dispensing, the kind and quantity of the drug dispensed, and the name and address of the patient to whom dispensed. Further, every physician, who has in his possession narcotics of the type covered by this law, must, whenever requested so to do by the collector of internal revenue of his district, make a true and correct statement to the collector setting forth the quantity of such drugs received by him during a preceding period not exceeding three months, the names of the persons from whom the drugs were received, the amount received from each person, and the date when received. Failure to comply with the provisions of this law shall, on conviction, submit the offender to a fine of not more than $2000 or imprisonment for not more than five years, or both, in the discretion of the court.

It must be remembered that most of the states have special antinarcotic laws, which differ somewhat from the federal act. Hence the physician is subject to the provisions of both acts, compliance being obligatory. As this Harrison Law was intended to prevent, as far as possible, the evils of indiscriminate sale and dispensing of narcotics and to curb the growing traffic in narcotic drugs, the physician should do all in his power to aid by seeing that his use of such drugs is limited to the dispensing and prescribing of them in good faith as medicines. Violation of the Harrison Law has been held to constitute gross malpractice.[1]

The above Harrison Narcotic Act was declared constitutional by the United States Supreme Court on March 3 1919,[2] although four of the nine justices dissented from the opinion. Doubt as to the correctness of this decision has recently been increased by a decision in the case of *United States v. Daugherty* rendered in 1926, the court saying: "The constitutionality of the Antinarcotic act, touching which this court so sharply divided in *United States v. Doremus*, 249 U. S. 86, was not raised below and has not been again considered. The doctrine approved in *Hammer v. Dagenhart*, 247 U. S. 251; *Child Labor Tax Case*, 259 U. S. 20; *Hill v. Wallace*, 259 U. S. 44, 67; and *Linder v. United States*, 268 U. S. 5, may necessitate a review of that question if hereafter properly presented." It is probable that, if the principles underlying the unconstitutionality of the Child Labor Tax Law and of the Future Trading Act are applied to determine the constitutionality of the Harrison Narcotic Act, this act is likely to fall. "Whether this would work an unmitigated evil is open to question. Moreover, no satisfactory evidence has yet been adduced to show that the Harrison Narcotic Act has accomplished or is accomplishing its purpose, the suppression of the narcotic habit. Statistics adduced to show that narcotic addiction is less prevalent do not and cannot take into account with any degree of accuracy narcotic drugs distributed through underground channels. Nor do such statistics connect even such diminution as some of them purport to show with the operation of the act."[3]

Prescribing and Use of Alcoholics.—Thanks to the 18th Amendment and the Federal Prohibition Act (Volstead Act), the physician is now restricted to a certain extent in his prescribing and use of alcoholic beverages. The provisions and regulations of the Federal Prohibition Act are so extensive and are so subject to change that we can give only a cursory survey in this place. According to the present interpretation

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[1] See Gregory *v.* McInnis et al. (S. C.) 134 S. E. R. 527.

[2] United States *v.* Doremus, 249 U. S. 86.

[3] See Editorial in Jour. Amer. Med. Assoc., 1926, **86**, 627.

(which is the subject of much controversy), any liquid containing ½ of 1 per cent. of alcohol is an intoxicating liquor, and its manufacture, sale, transportation, delivery, possession, etc., is prohibited, except as specifically provided in the Act. Medicinal preparations are regarded by the Prohibition Act as unfit for beverage purposes when they contain no more alcohol than is necessary for the purpose of extraction, solution, or preservation, and contain in each fluid ounce a dose as a whole, or in compatible combination, of one or more agents of recognized therapeutic value, and contain no agents either chemically or physiologically incompatible with the active medicinal agents.

A duly licensed physician in active practice, holding a permit from the Prohibition Director, may prescribe alcoholic liquors for medicinal use after careful physical examination of the person for whom the liquor is intended, or if such examination is impracticable, then upon the best information obtainable, when he believes in good faith that the use of such liquor is necessary and will afford relief from some known ailment. A physician, who does not hold such a permit can not, of course, issue prescriptions for intoxicating liquors. Only spirituous liquors (distilled liquors) or vinous liquors containing not more than 24 per cent of alcohol can be prescribed by a physician, and of these not more than 1 pint of spirituous liquor or ¼ gallon of vinous liquor on one prescription, or for any one person within a period of ten days, and the aggregate of the alcohol contained in the liquors thus purchased must not exceed ½ pint. It is clear, therefore, that ales and beers can not be thus prescribed. In this connection it is to be mentioned that physicians can not prescribe liquors for their own personal use or obtain liquor for such use upon their own prescriptions. All prescriptions must be made out, except in emergencies, upon special printed blanks consecutively numbered, issued by the Prohibition Director, and no physician may issue more than 100 prescriptions for liquor within a period of 90 days without special permission of the Director. This official prescription is not used for alcohol-containing medicines which are, as defined above, unfit for beverage purposes. The physician must make four copies of each prescription, two originals and two carbons, both original copies being given to the patient, while both carbon copies are retained by the physician. The patient gives both original copies to the pharmacist, who cancels both and during the month sends one copy to the local prohibition administrator, while the physician, within the first 10 days of each month, must send to the local prohibition administrator one of the retained carbon copies of the prescription. Further, physicians issuing prescriptions for alcoholic liquors must keep an accurate record on a form furnished by the Prohibition Director, showing the date of issue, to whom issued, the kind of liquor, the purpose or ailment for which prescribed, the quantity prescribed, and the amount and frequency of the dose, which record must at all times be open to inspection by officers of the law. The physician's prescription can be dispensed only by duly licensed retail pharmacists holding a dispensing permit, and no prescription may be filled more than once.

According to further provisions of the Act, physicians having permits for such purpose may obtain not to exceed 6 quarts of intoxicating liquor in any calendar year for administration to their patients for medicinal purposes, where delay in procuring the same through a pharmacist upon a prescription might result in loss of life, aggravation of the ailment, or intense suffering. Physicians may, also, obtain in any calendar year not more than 5 gallons of alcohol for use in compounding medicinal preparations and for purposes other than those of internal administration.

Most of the states have enacted Prohibition Laws, which for the most part follow the provisions of the Federal Law. However, it is wise for the physician to know fully the requirements of his own state relative to the use and prescribing of alcoholics, as he must comply with both statutes.

With respect to the validity of the above restrictions on the prescribing of alcoholic beverages by physicians several courts have given rulings, which would indicate that the restriction to a certain number of prescriptions in any given period is unconstitutional, as it is depriving both physician and patient of liberty without due process of law. It is highly probable that future legislation will change to some extent the provisions of the law as it now stands.[1]

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[1] See the opinions of the United States District Court in Montana (United States *v.* Freund, 290 Fed. R. 411), The District Court for the Southern District of New York (Lambert *v.* Yellowley, 291 Fed. 640) and the United States District Court in Ohio (Price *v.* Russell et al. 296 Fed. R. 263).

CHAPTER II

MALPRACTICE

Malpractice grows out of the implied or expressed contracts between the physician and his patient, as discussed in the preceding chapter. As viewed by the courts, it may be of two types, civil malpractice, which submits the practitioner to suits for damages personal to the patient, and criminal malpractice, which brings the physician into court to answer a charge of criminal responsibility.

CIVIL MALPRACTICE

This may be defined as the failure, on the part of the physician or surgeon (dentist, pharmacist, etc.) to exercise the care, skill and judgment, which the law requires and which the patient is lead to expect from the physician, so that injury to the patient, or even death, may result. This form of malpractice is not infrequently known as "Negligent Malpractice", as the basis of the action is the neglect of the physician in the treatment of the case or the failure to use proper diagnostic measures. While the physician or surgeon, when called to treat a case of disease or injury, is not to be regarded as a miracle worker in that he guarantees a cure of the disease or insures a proper return of an injured part to normal function and appearance, yet such cases of alleged malpractice do find their way into courts altogether too frequently. Although the physician must be considered as one having limitations, yet he does obligate himself, as we have already pointed out, to possess average and reasonable learning, skill and experience and to use reasonable and ordinary care and diligence in the exercise of this skill.[1] It must be remembered, in this connection, that a physician or surgeon cannot make a valid contract with a patient that the patient shall waive any claim for damages growing out of the physician's want of ordinary care and skill. In determining what constitutes reasonable skill, care and diligence, that possessed and exercised by physicians practicing in the same general or similar localities must be taken into consideration. It is clear that one practicing in a small rural community could not be expected to have the skill and experience possessed by one enjoying a large urban general or hospital practice. "The practitioner must possess at least the average degree of learning and skill in his profession in that part of the country in which his services are offered to the public; and if he exercises that learning and skill with reasonable care and fidelity he discharges his legal duty." Further, if a physician does not possess ordinary skill and experience, he can not have good judgment; but if he does possess such skill and experience, he is obligated to exercise his best judgment in their use. He can not legally be held for errors in judgment providing he has used proper care in arriving at such judgment, as the most skillful may err in judgment in advising a particular form of operation or in prescribing a special remedy. If such an operation or such a remedy be one that any practitioner, following the same system of practice as the physician in question, would or might use, then no blame attaches to the practitioner for the failure of his judgment in any particular case. However, if the physician failed to discover and rectify errors in his treatment, then he becomes liable. Thus in a decision of the Supreme Court of Oklahoma, the court said: "Negligence is not predicable on the non-success of a surgical operation when reasonable skill and ordinary care are exercised in its performance, nor is negligence predicable on error of judgment in the method of treatment when ordinary care and intelligence direct such judgment. But if, in the exercise of reasonable skill and ordinary care, it ought to be discovered that an injury or ailment does not yield to the usual and approved methods of treatment, the failure to discover this fact, or if discovered, a failure to acquaint the patient with that fact, will constitute negligence."[1]

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[1] See Dunn *v.* Beck (Mont.), 260 Pac. R. 1047.

If there is an established form of treatment for a special case, it is expected that the physician will follow it, departing from it at his own risk. If injury results from the employment of methods not recognized by the profession at large, the physician is liable for damages for such injury. If one experiments with untried remedies or operations, he does so at his own risk and must stand the consequences of his judgment and be able to prove to the Court that such treatment, although new or even original with him, is rational and can not be held responsible for the resulting injury or the failure to benefit his patient. In this connection it is to be repeated that the physician must use the most approved methods of diagnosis in his handling of the case, or run the chance of being charged with malpractice. Thus, the failure to use an X-ray examination in a case lead the Court of Appeals of Rouen to impose a penalty on the physician.[2] Whether or not this ruling was justified may be questionable, but it shows the possibility with which the physician may be confronted.

Whether the treatment adopted by a practitioner is or is not proper must be determined solely on the basis of the usage in the school of practice to which the accused belongs. The law recognizes no difference between these systems of practice and gives freedom of choice to the patient in selecting his own physician. Should harmful results follow, the patient can not legally maintain a suit for malpractice because a chiropractor, for instance, failed to adopt methods or prescribe remedies employed by the so-called regular practitioner. A physican is expected to follow his own school of practice and not deviate therefrom. It is the duty, however, of the follower of any particular system of practice to recognize whether or not his method of treatment is such as might be used in the handling of a specific disease. Thus, the Supreme Court of Michigan, in reversing a judgment entered on a verdict for the defendant (a chiropractor, who attempted to treat a case of diphtheria by his method) said: "While not registered, the defendant was a graduate of a chiropractic school. He assumed to treat human ailments only in accordance with the system taught in such school. This fact was well known to the plaintiff. The burden was therefore cast on her to show by competent evidence, not only that his treatment was injurious or not effective, but that the requisite care and skill was not exercised by him in administering it. It necessarily followed that such proof must be made by one engaged in treatment by similar methods to those employed by the defendant. With the merits of the several drugless systems of relieving human ailments, the courts have no concern. While the plaintiff knew the nature of the treatment administered by the defendant, she did not know whether such treatment would be efficacious to relieve the ailment with which the child was afflicted. It was the duty of the defendant to use reasonable care and skill so to ascertain. While he insisted that he and others of his school of practice did not diagnose cases or treat diseases, and said that he knew nothing about germs or the symptoms of tonsillitis, quinsy, or diphtheria, he did assume to relieve pain and suffering. When he undertook to administer treatment to the child, he assumed the responsibility of determining whether the treatment he proposed to administer, and afterward did administer, was such as might reasonably have been expected to afford relief. So to determine, it was incumbent on him to use reasonable care and skill to ascertain whether the ailments were of the class to which his treatment applied. If not, it was his duty so to advise the plaintiff, in order that she might secure the services of one familiar with such ailments. His neglect to use reasonable care and skill to ascertain whether or not the child had diphtheria, if established to the satisfaction of the jury, would sustain the charge of malpractice made by the plaintiff."[1]

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[1] Bungardt *v.* Younger (Okla.), 239 Pac. R. 469.

[2] See Jour. Amer. Med. Assoc., 1923, **81,** 1800. In Taylor *v.* De Vaughn (Calif.), 266 P. 960, failure to use X-rays in following the healing of fracture was malpractice.

While possessing reasonable skill and exercising due care, diligence and judgment in the use of this skill, it is expected that the physician will keep up with the advances of his profession in a general way and adopt measures which are generally approved by the profession of his school of practice. He is not expected to be a specialist in any particular line, but, if he does hold himself out as such a specialist, he must be judged by the practice of similar specialists and not by that of the general practitioner.

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[1] *Janssen v. Mulder* (Mich.), 205 N. W. R. 159.

Should a practitioner be asked to perform an operation or follow a line of treatment, which in his opinion is unnecessary or inadvisable, he should advise against it. If, however, the patient insists, the judgment of the physician is opposed. Should the surgeon now perform the operation or follow the treatment requested and should injury result, the practitioner can not be held liable, provided he has exercised ordinary skill and care in his work. However, it would be better in such contingencies for the physician to refuse to deviate from his own judgment rather than to follow the procedure which he feels is not warranted.

Surgical operations should never be undertaken without the consent of the patient. It occasionally happens, in emergency cases, that an operation may have to be performed without consent of the patient or a member of his family. If the operation is necessary to save life, no action can be taken against the surgeon. In order to avoid possibility of successful litigation for professed damages in surgical operations, where claim is made that certain organs were removed without the consent of the patient, it is wise for the surgeon to have a written consent for the operation stipulating that he shall do whatever in his judgment is necessary. This consent is usually to be obtained from the patient, or the parent, guardian, or near relative in case the patient is not in a condition to decide or is a minor child. The consent of the husband is not necessary to permit operation on a wife. In his examination of a patient, especially of a female, the physician should be careful to obtain consent for the examination. While the patient's consent is usually implied from the fact that she permits it, yet, if any objection be raised, the examination can not be made without the possibility of a charge of assault, even if the physician be requested to make the examination by a court of law.

As to responsibility for surgical operations it is generally held that the surgeon is responsible for the work of his assistants and nurses while they are acting under his direct supervision. Should a sponge be left in the abdomen, the surgeon may be held responsible, although this part of the work is usually checked up by one of the nurses who has charge of the sponge count.[1] The responsibility for the anesthetic rests with the anesthetist provided he be a skilled anesthetist, but if the surgeon asks an incompetent person to administer the anesthetic then the surgeon becomes responsible for any damage that may arise from its administration.

Contributory Negligence.—As stated in the previous chapter, the physician owes it to his patient to instruct him or his attendants as to the various matters connected with the handling of the case. It is the implied duty of the patient and his attendants to follow such instructions. If the patient or any of his attendants should, in any way, refuse to follow these directions or neglect to comply with the reasonable suggestions of the physician, or if the patient aggravates his condition by misconduct, contributory negligence is chargeable against the patient and his attendants and, in consequence, the physician is relieved of any blame that may attach for the resulting condition. Damages can not be collected from the physician under such circumstances. The burden of proof in a suit for malpractice is always on the plaintiff, who must show that there was a lack of skill, care and diligence on the part of the physician and the evidence on these points must, necessarily, be given by skilled and experienced physicians. The reputation of the accused physician should not be taken into consideration in such cases, as the question involved is limited to his handling of the specific case and has nothing to do with his care, diligence and judgment in other cases. Should the physician, on his part, be able to show contributory negligence, then the case will, in all probability, fail, as the plaintiff can not prove his necessary point.

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[1] See Ault *v.* Hall (Ohio), 161 N. E. 518.

CRIMINAL MALPRACTICE

By criminal malpractice is meant that the conduct (practice) of the physician is so unusual and so utterly lacking in ordinary prudence and judgment that great harm, or even death, results to the patient. Such acts may be either (1) wilful on the part of the physician or (2) those forbidden by express statutes. The wilful acts on the part of the physician may, perhaps, be without criminal intent, but they show such gross ignorance and negligence as to warrant a presumption of the criminal intent. If the consequences of the neglect are so marked or so fatal as to justify this presumption, the action of the physician will be regarded as criminal even though it is really nothing more than the result of negligence. Such cases are, fortunately, quite rare, but they subject the physician to criminal prosecution and may, also, constitute grounds of liability in a civil suit against him. The basis of the suit is that gross negligence is a misdemeanor and is punished criminally.

Besides the wilful or grossly negligent type of criminal malpractice, the law recognizes another form in the commission of acts forbidden by statute, toward a person under the care of the physician, as a result of which act the person suffers death or injury. The *first of this class* of case to be discussed is *criminal abortion*. The early common law did not recognize abortion as a crime if the mother consented to it. Later it was regarded as criminal only if the child had quickened. Still later, it was held that it was not the death of the product of conception that constituted the offense, but, rather, the stoppage of gestation. Now, in practically all of the states of the Union, Criminal Abortion is a statutory offense. If the abortion result in the death of the mother, the one performing the operation is held to be guilty of murder or manslaughter, on the ground that the operation is dangerous to life and has no lawful purpose, hence criminal intent is to be presumed. Further, if an abortion is attempted and the child is born alive but before it is really capable of separate existence and then dies, the one producing the abortion is guilty of manslaughter. It has been decided[1] that the woman on whom a miscarriage is produced is not criminally liable and is not to be regarded as an accomplice. However, there is no right of action between the woman and the physician who commits the abortion as has been decided by the court of Appeals of the District of Columbia.[2] If the woman fully understands the purpose of the operation and consents thereto, she is engaging in an unlawful and an immoral act. No court can lend its aid to one who founds her cause of action on an immoral or illegal act and, in consequence, the woman in such a case can not recover damages from the physician for alleged malpractice of a civil nature, although the physician may be proceeded against on criminal grounds.

If, however, an abortion is deemed by the physician, after he has had full consultation with brother physicians, to be necessary to save the life of the mother, it may be performed with no blame attaching to the physician. This is the so-called "Therapeutic Abortion". Although in some of the states there are statutes making the mother a party to the criminal action, in most states no liability attaches to her for causing herself to abort or for consenting to the operation by others (see preceding paragraph). Advising a woman as to methods of producing abortion will, in most cases, subject the physician to criminal liability if the advice be followed. The intent to produce an abortion is the leading point in the prosecution for criminal abortion. Should the statute not provide that the attempted abortion be upon a pregnant woman, it is unnecessary to prove pregnancy. Further, the viability of the fetus is not essential to the commission of the crime. The physician becomes criminally liable by the simple attempt to produce an abortion. This is the special reason why a physician should be guarded in his actions should a woman come to his office asking that an abortion be performed or after one has been started by others. In such cases he should protect himself by calling in consultation at once and, if intervention is deemed wise, he should notify the coroner as to the circumstances of the case.

A *second class of case*, coming under the head of acts forbidden by statute and subjecting the physician to prosecution for criminal malpractice, is the prescribing for or treating patients when the physician is intoxicated. If a physician, when under the influence of alcohol, attempts to treat or operate upon a patient, he places the latter in great jeopardy and must be held responsible for such actions. Under the above conditions, it may happen that proceedings may be instituted against the physician for revocation of his license to practice medicine.

[1] Thompson *v.* United States, 30 App. D. C. 352.

[2] Hunter *v.* Wheate (D. C.) 289 Fed. R. 604.

CHAPTER III

IDENTIFICATION OF THE LIVING AND THE DEAD

By identification (from the Latin *idem*, the same) we have reference to the determination of the characteristics which distinguish one person from all others, either during life or after death, or, in other words, the determination of the individuality of a person. In civil cases the identity of an individual often constitutes the entire subject of the dispute, while in criminal suits it may be the essential link in the chain of evidence. Cases of mistaken identity are constantly occurring in every day life, so that it is not infrequent to find them becoming the center of litigation. Upon the establishment of identity may depend, to mention only a few of the possibilities in the case of the living, a question of a marriage, of filiation upon which may depend the inheritance of large estates, the question of assumption of one's rightful position and property after years of absence, the maintenance of real or false claims to life insurance, the prosecution of an assailant in cases of assault, etc. In criminal cases, especially in those for murder, the law requires identification of both the victim and the alleged author of the crime. When the question of the identification of a recently dead body arises, or of one long buried or submitted to such processes as burning, treatment with chemicals, etc., all of the resources of the lay as well as of the professional witnesses may be taxed to the utmost to solve the puzzling points at issue. In such cases as the latter, the establishment of the identity of the individual, a part of whose remains have been found, may never be possible.

IDENTIFICATION OF THE LIVING

Identification of the living is, for the most part, concerned with those who have previously been convicted or at least examined by the police. Naturally if there is no record by which one may be guided, the question of identification must rest almost entirely upon the evidence of relatives, friends, neighbors, etc. However, as we shall see, the evidence of such persons may not be reliable at all times, so that physicians or medicolegal experts may be interrogated as to their knowledge of the absence or presence of bodily defects, markings, such as scars, naevi, tattoo marks, etc., or to testify as to the effects of climate, occupation, changed modes of life, etc. upon the appearance of the individual in question. The unreliability of trusting absolutely to identification by relatives and friends has been well expressed by Ewing[1] as follows: "The mutual recognition of friends who are associated at frequent intervals is a matter of daily occurrence which carries no thought of the principles on which rests an establishment of identity. Friends who have been separated for years usually require nothing more than a glance at the features to excite recognition and start a train of associations long since passed out of mind. The principle so fundamentally applied by Hume is here the basis of identification, for we know *by experience* that the possibility that another person, exactly resembling our friend, should appear under such circumstances need never be considered. If, however, the period of association shortens, or if the character of the association has been sufficiently prolonged to allow the change of time and occupation to stamp the features and estrange the mind, the recognition, even of former close friends, frequently requires the overcoming of surprise and momentary doubt. Instances of this sort are not infrequent where the ordinary changes in features, voice, and character reduce the basis of recognition of friends solely to a belief in their verbal statements. A distinctly new element is added to the problem when it is required to convince a third person of the identity of a friend, for the moment the question of a *proof* of such identity is raised by the third person a most delicate and difficult problem arises that has again and again taxed the finest sagacity of both lawyer and physician. This last situation always exists when the question of identity is brought before a jury, and the literature of legal medicine offers many famous instances in which the decision turned, often in an extremely dramatic way, upon the identity of individuals. It might be expected from the indirect nature of conclusions drawn from the experience of the senses, and from the still more uncertain character of personal impressions, that mere verbal statements, in the absence of objective proof, are of little positive value in deciding questions of identity."

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[1] "Identity" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, I, 132.

The literature carries some well-known cases which serve to point out the unreliability of all evidence based upon personal belief and experience, and which indicate the danger of accepting accidental physical resemblance as more or less positive proof of identity. One of the most interesting of these cases is that of Martin Guerre[1]. Guerre had been away from home for eight years and was presumably dead. An adventurer named Armand Dutille, who appears to have exhibited the closest possible resemblance in features and person to Guerre, passed himself off as Guerre and was accepted by Guerre's wife as her husband and took possession of the property. For three years he lived in the same house with four sisters and two brothers-in-law of Guerre without exciting their suspicion and children were borne to him by Guerre's wife. Finally Dutille's worthless character began to assert itself and aroused a train of suspicions which led to an indictment of the impostor. The legal inquiry, however, remained doubtful, or favorable to the impostor, until the real Martin Guerre appeared upon the scene, completely established his own identity and secured the conviction of the adventurer. An examination of the account of this very remarkable case not only discloses the unreliability of individual impressions about identity, but also in a marked degree illustrates the uncertainty of all forms of evidence of the most objective nature. Not only was Dutille's claim actively supported by Guerre's wife and relatives, but he showed many of the physical peculiarities of the other, such as scars on the face, a single blood-shot eye, and four warts at identical points on one hand. His mental caliber and composition were somewhat similar to Guerre's; he accurately recalled many of the early experiences of Guerre, and even possessed family relics known to have been carried away by the absent man.

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[1] Brought before the Parliament of Toulouse in 1560 and cited by Foderé, *Traité de Méd. Légale*, vol. i, chap. 2 and quoted from the Causes Célèbres by Mejan.

Another very instructive case is that of Sir Roger Tichborne.[1] A man, thought to be Arthur Orton, claimed to be Sir Roger Tichborne and heir to the baronetcy and estates of Sir Roger, who was believed to have perished at sea in 1854. In spite of the most striking dissimilarity finally demonstrated between this man and the real Sir Roger, the impostor was accepted by a score of witnesses, including seventeen servants, the family solicitor, and even the mother of Sir Roger, who positively identified him as her son. It was only when the objective points in the stature, features, and accidental markings of the body, as well as the mental traits of Orton, were compared with those known to have characterized the real Roger that the comparative worthlessness of the very positive impressions of the friends and even of the mother's instinct was established and the impostor detected.

Many other cases of mistaken identity might be mentioned, but we will pass this point with simple reference to the case of Hedden cited by Hamilton[2] and the cases of Adolf Beck and of George Edalji, detailed by Glaister,[3] both of whom were wrongly convicted of crimes which they did not commit.

Although it is very rare to find two individuals, who are exactly alike in all respects, yet that such similarities do occur is evident from a consideration of the evidence in the Guerre-Dutille case cited above. It becomes necessary, therefore, in solving the question of the identity of an individual, to employ methods of identification which are somewhat more fixed and definite than those of mere physical and mental characteristics. These methods as they influence the identification of the living might be discussed under the headings (1) Identification for Criminal Purposes; and (2) Identification for Civil Purposes. As these methods are, for the most part, a matter for the police rather than for the medical jurist, we shall give only a brief discussion of them at this time.

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[1] See Guy, *Forensic Medicine*, p. 686.

[2] *System of Legal Medicine*, 1894, I, 201.

[3] *Medical Jurisprudence and Toxicology*, 1921, p. 100.

In the identification for criminal purposes it is self-evident that, if the accused be an old offender, certain of his physical characteristics will have been recorded, so that comparisons may be rapidly made.[1] Should, however, the accused be a first offender, no records are available upon which to establish his identity and will not become so until his accusation and conviction, with the exception, of course, of what civil records there may be. The systems of identification for criminal purposes all depend upon the possession of certain records and descriptions, which enable the authorities to investigate and possibly establish the true identity of an accused individual. If the description of the criminal is very complete and covers the characteristics, which make it possible to recognize him *on sight*, it is given the name of *signalment*. This signalment may consist of a very detailed description of the physical and other characteristics of the individual and is so recorded that it may be easily and quickly found in case of need.

Pictures and Photographs.—The oldest means of identification, and certainly one of the most uncertain, is the picture. Recognition of an individual by means of his personal photograph appears a most simple process. However, it not infrequently happens that individuals are not recognized from their photographs or, on the other hand, certain persons are identified from a photograph which is in reality not their own. It is possibly true that certain anatomical characteristics of the face and head may give some valuable information as to identity, but such features may, at times, be entirely changed or distorted by the retouching of the picture, by the cut of the hair, wearing of a beard, etc. In the Tichborne case cited previously, there was a striking dissimilarity between the claimant and the real Roger, the photographs of the two contestants produced in court showing distinguishing peculiarities of eyes, ears, nose and mouth, and yet the false claimant was positively identified by a number of servants and even by the mother as the real heir.

If photographs are to be used in establishing identity, it is wise to insist upon the examination of the original, not retouched plate if this can possibly be obtained. This photograph must be sworn to by the photographer as that of a certain definite person and the date of its taking should also appear, as this latter fact may play a role in the determination of certain differences observed after a lapse of time.

In the taking of pictures for criminal purposes, much more detail may be obtained than is possible with the ordinary photograph. Each subject is photographed in two poses, one showing the right-sided profile and the other a full view of the face. These two views are complementary and permit of exact geometric reconstruction of irregularities and peculiarities of the subject. In such pictures identity may be proven by the finding of some really individual peculiarities, but most certainly not from any general resemblance which may be shown.

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[1] See "Identification of the Living" by Bertilion, *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, I, 63.

Anthropometric Signalment.—This system, which was originated by Bertillon, consists of the recording of certain bodily measurements and the filing of these records on cards in a specially arranged cabinet. According to the latest contribution of Bertillon, the important measurements, given in an order of decreasing signaletic value are as follows: (1) The length of the head, that is the maximum antero-posterior diameter, measured by a caliper graduated in millimeters from the concavity of the bridge of the nose to the occipital protuberance; (2) the maximum biparietal cephalic diameter; (3) the length of the left middle finger from the extremity of the finger to the metacarpal articulation; (4) the length of the left forearm measured from the point of the ulna to the extremity of the phalanx of the middle finger; (5) the bizygomatic diameter; (6) the total height of the body. There are certain other measurements

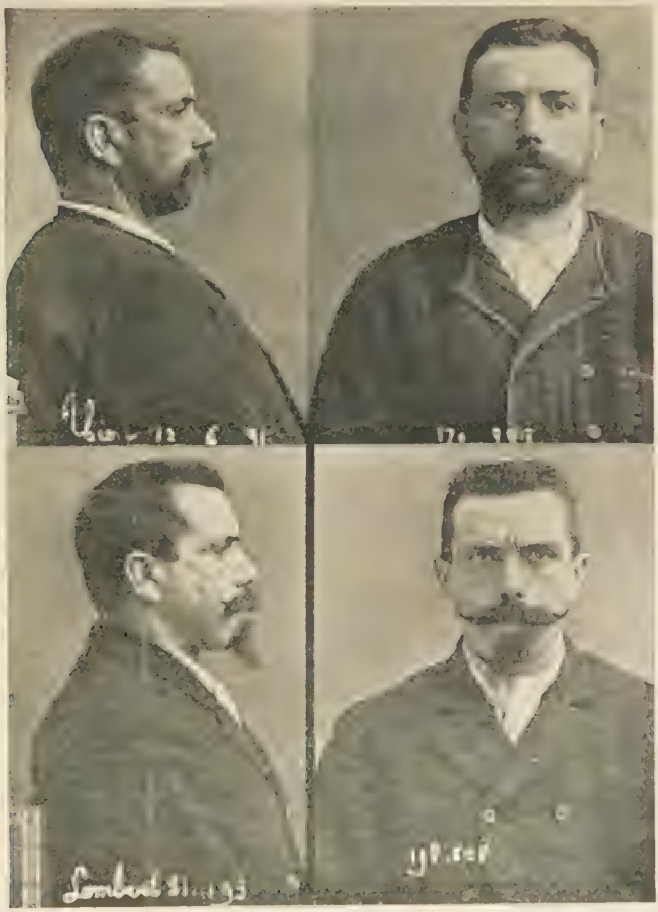

FIG. 1.—Photographs of the same individual at an interval of two years. Physiognomonic differences resulting from alterations of the beard and hair. (From Bertillon in Peterson, Haines and Webster "Legal Medicine and Toxicology.")

which may be taken, such as the span of the outstretched arms, the height of head and trunk, the length of the left foot, the length of the left little finger, and the length and breadth of the right ear, but these are not regarded as of such importance as the 6 above mentioned. As fast as these measurements are taken, they are entered upon a form, the front page of which bears the statements of the civil status as furnished by the subject, while the back of this form shows his photograph in the two views mentioned, the color of the left iris and a minute description of the peculiar marks presented by the individual with a rigorous indication of their form, dimension and situation. Finally, the prints of the 10 fingers are placed in the spaces reserved for them.

Descriptive Signalment.—By this we mean that the description of the individual characteristics is so detailed and minute that one has before him a descriptive photograph, a so-called "verbal picture" for purposes of identification. Practically every part of the body is described in such terms that nothing is left for the imagination. These analytic descriptions employ, for dimensions, the modifying terms small, medium, and large; for points relating to shade, the expressions clear, medium, and dark; for form, an appropriate vocabulary especially graded to permit the notation and classification of intermediate or average terms. The descriptions of the organs are given in terms relative to both form and dimension. Bertillon states that "During the twenty years in which instruction in the 'verbal picture' has been given regularly to the agents of the Parisian police and to those of the regional brigades of mobile police, cases of mistaken identity in the course of making arrests have completely disappeared."

Special Marks.—Special markings which appear upon the body are, oftentimes, of the greatest importance in solving questions of identity either for criminal or civil purposes. Practically every one has, somewhere on his body, one or more marks, such as moles, cicatrices, etc. It is clear, therefore, that if any value is to attach to the mention of certain special marks as found on the body, such marks must be carefully localized and exactly described. Even then they do not necessarily prove the identity of an individual, as two persons may show almost identical marks in the same location, as for instance, in the Guerre-Dutille case previously cited both claimants presented similar scars on the face and four warts at identical points on one hand. Hence, it is evident that all of the marks found on the body should be described, as the most insignificant one may be the most important in corroborating other proof of identity. It is extremely unlikely that two individuals will be so alike as to have every mark on their bodies agree as to location, size, form, etc. Of course, it is possible that certain marks found on the body may have come there after the time when the individual was criminally examined or was last seen by friends or relatives, or that old marks may have been effaced either by time, accident, or intent, so that former identifying marks may not always prove of great value. That such marks have, however, served their purpose in establishing identity is sufficiently attested by the court records of all countries.

Scars.—Very few individuals are entirely free from scars of some type or other, such as cicatrices of cuts, wounds, furuncles, etc. While scars in themselves have no special value, yet the careful and exact description of their form, location, and size may serve to differentiate them from similar scars found on others. In connection with the study of scars, certain questions, of great medicolegal importance, usually arise which must be answered in order that light may be thrown on their relation to identity either of the living or the dead. These questions have been so well answered by Ewing[1] that we quote largely from his presentation.

1. *Does a wound necessarily leave a cicatrix?* It is commonly stated that all wounds involving loss of substance necessarily leave scars. But this very general rule is an inadequate answer to the question in hand, for some wounds involving loss of substance do not leave scars, while others without loss of substance produce permanent cicatrices. The solution of this question requires the application of the ordinary laws of the repair of tissue after a division of continuity or loss of substance. When there is a loss of substance in an epithelial tissue, either skin or mucous membrane, which does not pass below the level of the epithelium, repair is effected by simple proliferation of epithelial cells and no cicatrix is formed. When the lesion involves other deeper tissues, subcutaneous connective tissue, fat, etc., the process of repair follows one of three plans: there may be healing by primary intention, by secondary intention, or the wound fills up from the bottom with granulation tissue. Upon the amount of granulation tissue formed will depend the extent and permanence of the scar, for this tissue is never entirely replaced, but becomes converted into dense cicatricial connective tissue. Any wound the healing of which has not occurred entirely through primary intention, but has been attended with suppuration or infection, will, in every case, leave an appreciable scar. If, however, the wound heals through primary intention, it is possible for an incised wound, even though associated with loss of substance, to leave no demonstrable permanent cicatrix.

2. *May scars be obliterated by time or by artificial means?* Clean, linear, incised wounds of which the edges are properly apposed, and in which the healing process occurs without suppuration or excessive exudation, leave thin delicate scars that may gradually disappear. On the other hand, there is no reliable evidence that a cicatrix formed after considerable granulation or suppuration has ever spontaneously disappeared. The prominence of delicate scars left after primary union may be considerably diminished by prolonged treatment with massage, but the larger or deforming scars may be removed only by excision, by which process the resulting loss of tissue is almost invariably sufficient

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[1] See article on "Identity" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, I, 154 et. seq.

to produce an indelible, although, perhaps, less prominent cicatrix. The small indistinct scars may be made somewhat more noticeable by friction of the surrounding parts or by the application of heat, both of which measures cause hyperemia in the normal tissues but not in the cicatricial tissue.

3. *Can the age of a cicatrix be inferred from its appearance?* The answer to such a question must be given guardedly and must have relation to the particular case at hand. We may, however, generalize as follows: With very rapid healing of incised wounds it is stated by Thoma that the incision may be invisible at the end of three days, although firm union has not yet occurred. In ordinary incised wounds the process of healing is usually complete in two weeks, leaving a soft, hyperemic, red cicatrix. Healing by granulation always requires more time than by adhesion. When there has been extensive loss of substance, as in lacerated and contused wounds; when the edges are imperfectly approximated or are drawn apart by underlying muscles, by movements of joints, or by the restlessness of the patient; and, especially, when there have been infection and suppuration in a wound—union proceeds more or less by granulation, and the formation of a cicatrix requires much longer time. The external appearance of a cicatrix varies much at different periods of its organization. A fresh scar is soft, tender, may often be broken down by firm pressure, and is reddish brown in color. At a variable period, usually not before a month or six weeks, the blood vessels and connective tissue begin to contract, the cicatrix becomes firm and takes on a brownish color. After months or years it may have nearly disappeared, and the connective tissue is contracted, leaving a white, glistening, hard, insensitive scar.

4. *Can the nature of the wound be determined from the character of the scar?* Much may be inferred, and some positive conclusions may be drawn as to the mode of origin of a wound, by an examination of scars. Accidental wounds produced by crushing force and attended with laceration and destruction of tissue give large, irregular, depressed scars. Bullet wounds, when produced by a weapon held within a few inches of the body, produce scars that are larger than the bullet, irregular in shape, and usually surrounded by indelible powder-stains; when a bullet wound has been produced from a distance, the scar is depressed, discoidal, and smaller than the bullet; in either case the scar at the point of exit of the bullet is larger than the scar at entrance. Stab wounds leave triangular scars, smaller than the blade. Burns, when of sufficient intensity to cause death of tissues below the epidermis, are followed by irregular, flat, smooth cicatrices, corresponding in size to the original lesion. Surgical wounds usually result in clear linear cicatrices, but suppuration, extensive removal of tissue, and prolonged use of drainage tubes may alter their appearance.

5. *Can the size of the original wound be determined from the scar?* The general rule is that a scar is always smaller than the original wound

owing to the contraction of the scar tissue in the long diameter of the areas involved. This contraction increases, up to a certain limit, with the age of the scar. Exceptions may be noted in the case of some wounds inflicted in childhood, as vaccination scars, linear operation wounds, naevi, and the scars resulting from their removal have all been observed in children to increase in size with the natural growth of the body.

Naevi.—These birth marks are usually permanent and seldom lose their sharp outline, though they may change somewhat in the early years of life. To remove such marks recourse was formerly had to such procedures as cauterization, excision, and other measures, but indelible scars were left in their places. At the present time electrolysis removes practically all traces of these often disfiguring marks, without leaving behind any indications of the operation. For purposes of identification these naevi should be very carefully described, their location, form and size being especially noted.

Tattoo Marks.—By tattoo marks we mean any sketch, design or spot resulting from the deposition under the epidermal layer of the skin of a more or less unalterable substance either of mineral or vegetable origin. The method of tattooing consists in pricking, point by point, into the skin with needles soaked in a solution of the dye desired. The bluish colors may be due to indigo, Prussian blue, or the common inks; the black dyes to India ink or other mixtures containing carbon; while the red tones are usually given by vermilion. Occasionally we find factitious or accidental tattooing from nitrate of silver, gun-powder, coal dust, bits of steel, etc. In describing any of these tattoo marks, found upon a body either living or dead, the form, dimensions, type and location should be as exactly given as possible, so that there may be little or no confusion with similar marks found on others.

It is clear that the permanence of these tattoo marks will depend upon the depth to which the dye is introduced and, also, upon the type of dye employed. That such marks may spontaneously disappear is attested by Casper who reports that out of 37 cases examined, 4 had completely disappeared, 3 had faded and 2 had partially disappeared; while Hutin states that of 509 cases studied at periods between 30 and 60 years after the marks were made, in 47 there was no trace of such marks. If the dye be introduced into the connective tissue layer of the skin, the marks will remain permanent unless some markedly destructive agent is used, when a scar will take the place of the tattoo mark. It is certainly true that all evidence of the most intense dyes may be removed by artificial means, such as blisters, escharotics, glycerol of papain, or by surgical procedures, but all of these methods result in scar formation. Shie[1] recommends the method of Variot as being the most reliable for removing these marks. This method consists in tattooing the old mark with a solution of 50 per cent tannic acid followed by rubbing the treated area with stick silver nitrate. It is to be remembered that the type and design of the tattoo mark may be changed by re-tattooing a larger or different design over the old one. Certain skin lesions, such as confluent small-pox, may obliterate these marks and Ewing is inclined to believe that severe eczema or psoriasis might also obscure superficial markings.

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[1] Jour. Amer. Med. Assoc., 1928, **90**, 94.

Occupational Markings.—The study of certain markings upon parts of the body, which are subjected to constant exercise of the same group of muscles or to the pressure and rubbing of tools in the every-day life of the individual, has lead, in certain cases, to the identification of the person as a follower of a certain trade, although perhaps more frequently such evidence is merely of corroborative value. These marks appear in the form of callosities, roughenings, stains, exaggerated development of certain muscles, and, occasionally, deformities. As most trades are associated, to a more or less extent with such marks we mention only a few of these to show the general types. Those engaged more or less constantly in writing frequently have a slight callosity on the tip or ulnar border of the little finger with a similar thickening of the epidermis where the pen is grasped between the index and middle finger; jewelers may show slight retraction of the last phalanx of the left thumb; dressmakers show a characteristic sign on the left index finger where the skin is roughened by multiple needle punctures; shoemakers suffer frequent cuts from the thread in the skin of the index finger between the second and third phalanges, the nail of the left thumb is usually thick and hard and its edge frequently serrated or broken; engineers show a callosity at the junction of thumb and forefinger of the left hand and there may be a series of callosities on the projecting surfaces of the palmar aspect of the fingers and palms of the right hand, as Cathcart has shown. Such marks are rarely found on the hands of the criminal classes as members of this group are not given to hard legitimate labor which might lead to such identifying indications, although forgers, counterfeiters and such may show marks and stains which may prove of value in identification.

Finger Prints.—As is now well-known, the epidermis of the tips of the fingers is characterized by fine lines, ridges and hollows which together form patterns, which are very permanent in form and are of sufficient distinctiveness in each person to warrant their use as a means of identification. These markings retain their individual peculiarities in the same person from infancy to old age, although their clearness may, in some cases, be slightly obscured by constant friction of the every-day life.

Purkinje, in 1823, first called attention to these peculiarities of the skin of the finger tips and described 9 standard patterns, but it was not until 1877 that their use as a means of identification was adopted by Herschel in connection with the natives of India and later, in 1890, Tabor proposed this method for registration of the Chinese in California. For criminal purposes Herschel was probably the first to suggest their employment but their real classification for such uses was first worked out by Galton in 1892. He demonstrated that absolute confidence could be placed on the permanency of the patterns and believed so strongly in the individuality of the markings that he calculated the chance of two prints being identical in two individuals as less than one in sixty-four billion. He called attention to the similarity of the finger prints of members of the same family, especially of twins, but showed that there were always some distinguishing points that could be brought out by close study. The surface area of these tracings enlarge somewhat with the growth of the individual, but the relations of the lines, their number, variable method of curving, etc., remain the same in the same person. This system was later elaborated and improved by Henry, whose classification is now universally employed.

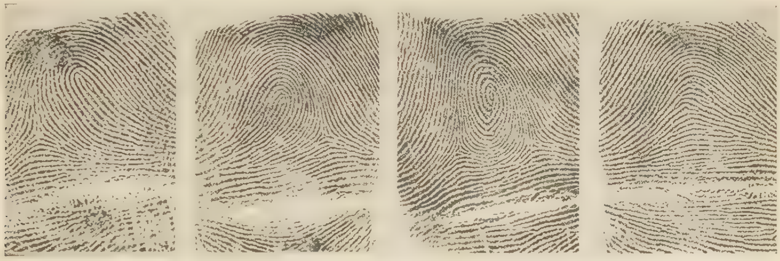
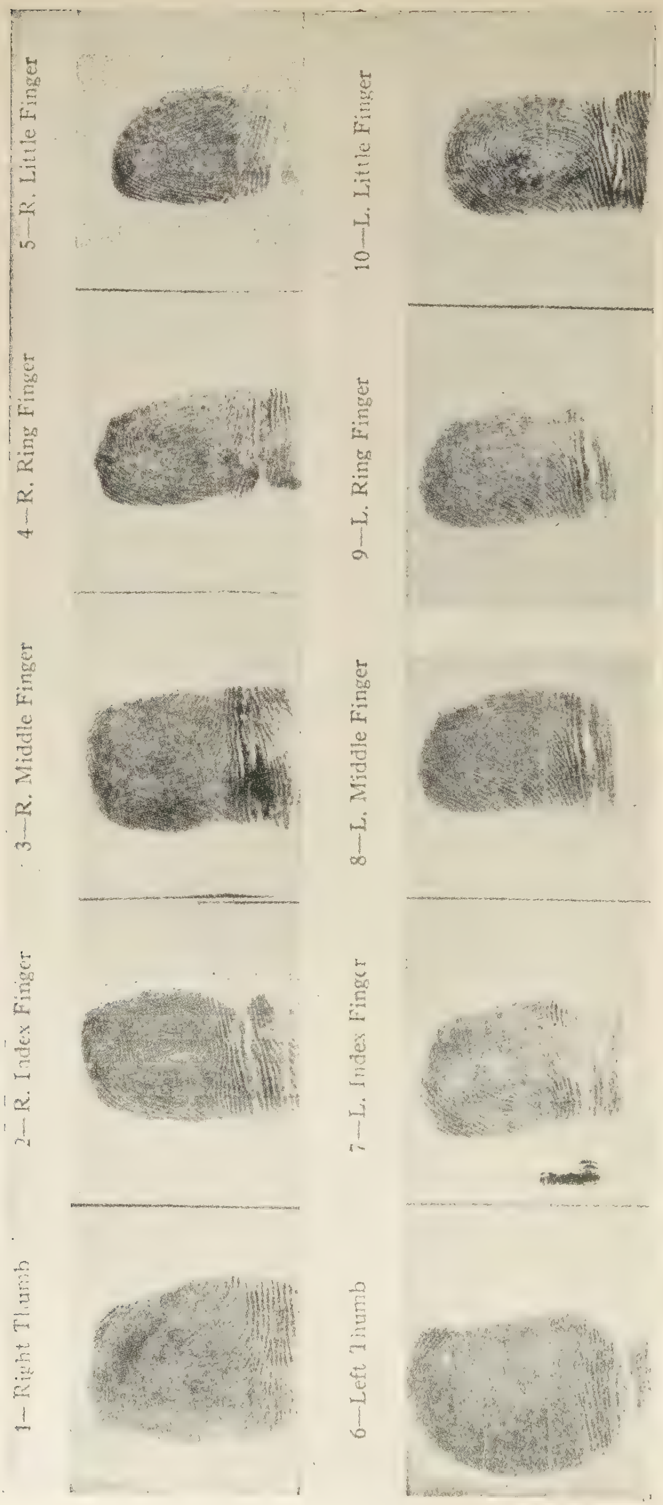

Loops oblique to the right. Form E.
Loops oblique to the left. Form I.
Circles (whorls), spirala, scroll-like forms. Form O.
Arched types. Form U.

FIG. 2.—Specimens of the four fundamental forms of finger-prints (right hand). (From Bertillon in Peterson, Haines and Webster, "Legal Medicine and Toxicology.")

The method of preparing these prints is simple and, in brief, is as follows: The surface of a copper plate or of well polished zinc, tin or even of window glass is lightly smeared with printers ink and spread out in an even layer by means of a small roller. The extremities of the fingers are now pressed on this inked surface so as to coat the fingers with the ink and the impression is then transferred to well glazed paper. These imprints are placed on the paper in two ways: (1) by a rolled impression, which consists of rolling the stained finger tip from without within on the surface of the glazed paper, thus obtaining the whole pattern with its various relations; and (2) by a plain impression, which consists simply of the imprint of the finger tip laid down on the paper without any movement whatsoever. The former prints are much preferable, although it is customary to employ both methods so that one may have prints for comparison with those that may arise in medicolegal inquiries. The prints of each finger and thumb of each hand are taken separately and placed in the proper position on the cards kept for this purpose.

In the classification of Henry there are 4 chief types of pattern: (1) the arched forms; (2) the loops; (3) the whorls; and (4) the composites. The arched forms are those in which the ridges pass from one side to the



1—Right Thumb
2—R. Index Finger
3—R. Middle Finger
4—R. Ring Finger
5—R. Little Finger
6—Left Thumb
7—L. Index Finger
8—L. Middle Finger
9—L. Ring Finger
10—L. Little Finger

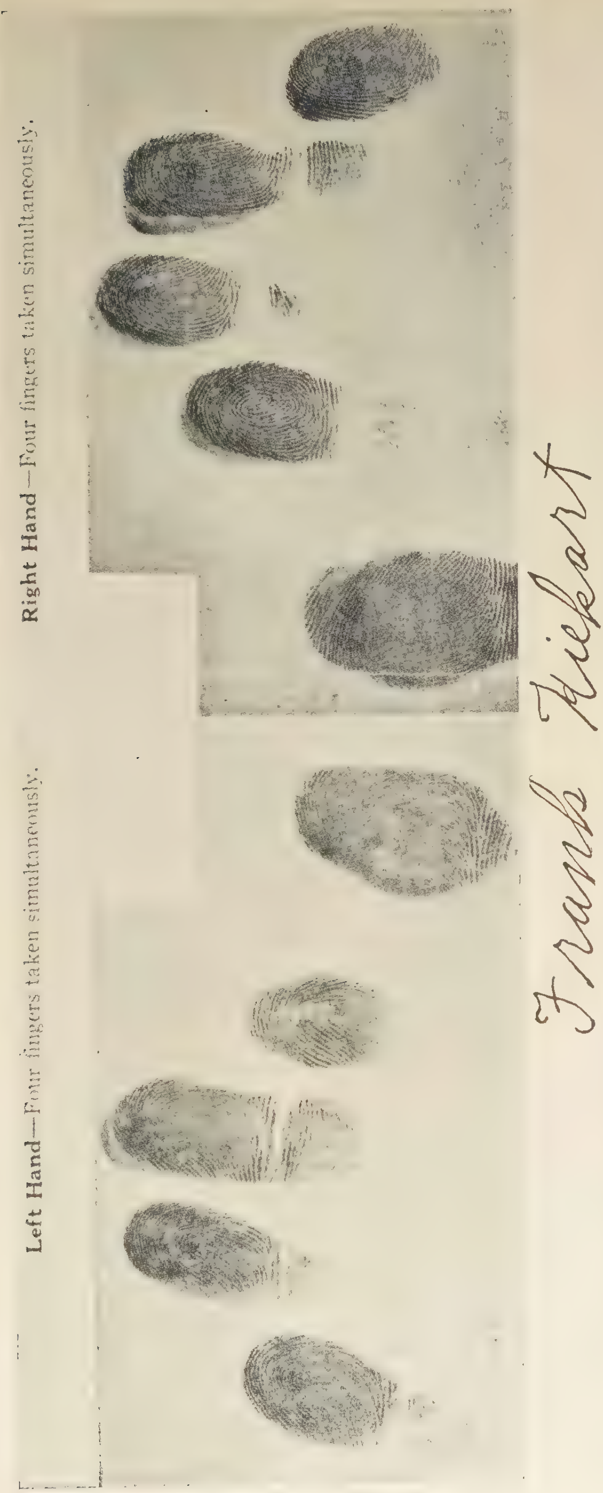

Right Hand—Four fingers taken simultaneously.
Left Hand—Four fingers taken simultaneously.
Frank Kiekart

FIG. 3.—Finger prints and signature of Criminal. (Courtesy of Homicide Bureau of the Chicago Police Department.)

other without making any backward turns; the loops show backward turnings but without any twists, the turns being either to the right or left, that is toward the ulnar or radial side of the hand; in the whorls some of the ridges make a complete circle in turning; while in the composites we have mixtures of the above types. Out of every 100 average impressions, 60 belong to the loop type, 35 to whorls and composites, and 5 to the arched forms. (Fig. 3.)

This finger print system of identification has been adopted in most of the Bureaus of Identification in all parts of the world and is in use in practically all armies of the world. For criminal purposes it is of value in establishing the identity of an old offender or, if finger prints are found at the place of commission of a crime, in showing the association of a suspected person with the crime. For civil purposes it has great possibilities in authenticating such documents as birth and death certificates, life and accident insurance policies, promissory notes, mortgages, etc.

Foot Prints.—Such marks obviously do not have as much importance as finger prints, as they are by no means as characteristic. However, it is occasionally possible to establish identity by their use. A foot print evidently will vary depending upon the material upon which the print is made and, also, upon the rapidity of progression of the individual. As Tidy shows, when the material is composed of freely movable particles, such as sand, the mark is usually smaller than the foot, while in clay or other similar material the print is always larger than the foot. The foot print of a person running is smaller than that of the same person walking, which in turn is smaller than that produced when standing. The peculiarities of the foot or shoe which has made the print will appear clearly, if the material upon which it is found is such as to take the impression. Thus, peculiar nail marks, absence of nails, cleats, holes in the sole, etc., may prove of importance in comparing the print with the shoe of the suspected person. If the print be made with the naked foot, the peculiarities of the foot, such as callosities, flat-foot, bloody cuts, etc., may be of some value.

In using foot prints as evidence, it is wise to make casts of them by warming the surface of the print and scattering over this surface stearic acid or paraffin, in which case the wax melts and forms a cast of the print, which may be removed when cool and taken away for future reference and preparation of plaster casts if deemed necessary. For making casts of prints in snow, gelatin often proves satisfactory as this medium may be easily melted and, when it is about ready to solidify, poured into the print without melting the snow and destroying the print.

Handwriting.—While the careful study of handwriting may, in the hands of an expert, reveal certain peculiarities and characteristics, yet such distinctions are rarely sufficient to establish identity, as it must be remembered that any special bit of handwriting produced in evidence may have been intentionally varied by the writer to cover up his identity.

However, if such a person be required to write rapidly some set subject-matter, the peculiarities in his known style may be revealed. For the medical man, however, testimony as regards handwriting is not concerned with types of identification. What he may be called upon to identify may be signatures to a will or other document, both as to that of the testator and of the witnesses, which signatures may have been made in his presence. Further, he may be asked his opinion as to the possibility of a paretic, for instance, having written a certain letter, document or will. The characteristic paretic writing may or may not appear in the writing under investigation.

Mental Qualities.—The mental and normal capacities of an individual, and especially his memory, may offer the most convincing proof of identity or of non-identity. "The conclusions drawn from facts thus brought out are all the more trustworthy, because they depend upon the reason and not upon the senses and because the influences affecting the ordinary laws of mind are very few compared with the limitless number of possible exceptions to physical laws." In the Guerre-Dutille and Tichborne-Orton cases, marked variations in mental qualities and especially as concerned the memory were large factors in finally establishing the falsity of the claims of Dutille and of Orton.

IDENTIFICATION OF THE DEAD

It is clear that some of the methods previously discussed may be employed in the identification of the dead. However, the questions arising in case of the dead are, oftentimes, much more difficult of solution. The general problem involved here relates almost exclusively to a study of the physical characteristics of the individual, which may have been markedly altered by disease, decomposition or mutilation. Further, a solution of many of the puzzling questions may necessitate a close examination of the viscera and the bones of the dead person. Thus, it may be required to determine the age, sex, and other characteristics of a body decomposed by long burial, by chemicals, or by burning, or of one greatly mutilated; to identify certain bones found in the neighborhood of a crime as of human origin; or to reconstruct the general stature and physical peculiarities of an individual from portions of mutilated remains. In a study of the identity of a dead body, the questions at issue have reference chiefly to a determination of the age, sex, stature and bodily peculiarities in relation to those of some specific person known to have been alive.

Age.—In the *living* person the age may be determined in a general way within certain limits. Thus we say that a person is in the period of infancy, youth, adult life, or old age. However, here we may be much misled by outward appearances as precocious development of the young, premature old age in the adult, or marked virility of the aged may occasionally vitiate our calculations. Thus, in infancy consideration of height, weight, number of teeth, general development and other factors may permit of more or less accurate conclusions, but it must be remembered that all of these elements are influenced by malnutrition and syphilis on the one hand and by precocious development on the other. In youth we add to the above factors the signs of puberty, but find that marked variations in the time of establishment of these bodily characteristics prevent an accurate determination of the age. In adult life we notice that personal inherited peculiarities, strictly healthful mode of life or dissipation, worry and cares of business or of the struggle for existence, disease, appearance of gray hair, and early onset of arterio-sclerosis may so change the appearance of an individual that he may retain his youthful characteristics for a long period or, what is perhaps more common, may seem much older than he really is. So, too, we find the conditions much the same in old age, many elderly people appearing younger and many much older than they actually are.

As a general rule the age in the young is quite accurately determined by a study of the development of the teeth and by the progress of ossification in the different bones. However, the retarding influence of hereditary characteristics, as well as of rickets, malnutrition and syphilis, must be remembered, as also the accelerating influence of precocious dentition. The temporary or milk teeth are 20 in number and, on the average, appear as follows: The 4 central incisors from 5 to 8 months; 4 lateral incisors from 7 to 10 months; 4 anterior molars from 12 to 15 months; 4 canines from 14 to 20 months; and 4 posterior molars from 20 months to 3 years. These temporary teeth begin to be shed from the fifth to the seventh year and are replaced by the permanent teeth as follows: The 4 anterior molars at 6th to 7th year; 4 central incisors at 7th to 8th year; 4 lateral incisors at 9th year; 4 anterior bicuspids at 10th year; 4 posterior bicuspids at 11 years; 4 canines at 12 to 12½ years; 4 second molars at 13 to 14 years; and 4 posterior molars (wisdom teeth) at 18 to 24 years. The exact period of eruption of all of these teeth may vary but, probably, the greatest variation is noted in the case of the wisdom teeth.

A study of the centers of ossification and of the progress of ossification is of great value in arriving at an approximately accurate estimate of age. As Ewing remarks "Barring certain exceptions to be attributed to rachitis and syphilis in youth and to osteomalacia, gout and rheumatism in adult life, the union of the various epiphyses of the long bones and the complete ossification of the shafts proceed in a very uniform sequence and careful observations on the condition of the epiphyseal lines and ossification zones in the skeleton are the chief guides in determining the age of a dead body or of mutilated remains." It is to be recalled that the bones and the extent of union of the epiphyses may be quite as well examined, either in the living or the dead, by means of the *x*-ray as by dissection. The approximate periods of the union of epiphyses and processes of the bones is here outlined, as adapted by Ewing from Quain's Anatomy.

First Year.—Laminae of some vertebrae; petromastoid and squamous portions of temporal; great wings and body of sphenoid.

Second Year.—Laminae of lower sacral vertebrae; upper and condylar portions of occiput; frontal suture; lateral halves of inferior maxilla.

Third Year.—Basilar and condylar portions of occiput; fontanels nearly closed.

Fourth Year.—Basi-occipitals and exoccipitals; odontoid process of axis; fontanels closed.

Sixth Year.—Laminae of upper sacral vertebrae.

Seventh Year.—Rami of pubes and ischium.

Sixteenth Year.—Lower epiphysis of humerus; coracoid process of scapula.

Seventeenth Year.—Upper epiphysis of radius and ulna; lesser trochanter.

Eighteenth Year.—Internal condyle of humerus; greater trochanter; head of femur; lower epiphysis of tibia.

Twentieth Year.—Greater tuberosity of humerus; lower epiphysis of radius, ulna, femur, and fibula.

Eighteenth to Twentieth Year.—Parts of acetabulum; auricular plates of sacrum; sphenoid and basilar portions of occiput.

Twenty-first Year.—Upper epiphysis of tibia.

Twenty-second Year.—Acromion and scapula.

Twenty-third Year.—Tuberosity of ischium; symphysis pubis; anterior inferior spine of ilium.

Twenty-fourth Year.—Upper epiphysis of fibula.

Twenty-fifth Year.—Heads and tuberosities of ribs; sternal epiphysis of clavicle.

Thirtieth Year.—Three coccygeal vertebrae.

Middle Life.—Union of coccyx and sacrum; greater cornua and body of hyoid.

Sex.—In the living a decision as to the sex of the individual usually offers little difficulty. However, in cases of true hermaphrodism doubt may arise, so that the settlement of such questions as inheritance, for instance, may be difficult. As sex really depends on the presence of testicles or ovaries, the point may be proven by seminal emissions after puberty or by menstruation. Where decomposition has destroyed the external and internal evidence of sex organs in a dead body or where extensive mutilation has occurred an absolute proof may be difficult although much may be determined. Thus, if a head be examined the character of the skin, the type of hair, indications of a beard, etc., would all be of value; with the trunk, the broader shoulders and more muscular development of the male, the shape of the chest and evidence of compression of the ribs in the female, would carry some weight; while with the arms or legs, the size of the bones, the formation of fingers or toes, the size of the hand or foot, and the extent of muscular development would all be considered.

As regards the skeleton, there are marked differences noted in the two sexes. The bones of the female are lighter than those of the male; the lower jaw is relatively smaller and lighter, the mastoid processes and zygomata are less prominent, the thorax is relatively shorter and more rounded and the spine is relatively longer in the female than in the male. The pelves differ in many respects. According to Quain "In the female the height is less and the breadth and capacity of the true pelvis greater; the ilia are, however, more vertical, and thus the false pelvis is relatively narrower than in the male; the inlet of the true pelvis is more regularly oval, the sacral promontory projecting less into it; the sacrum

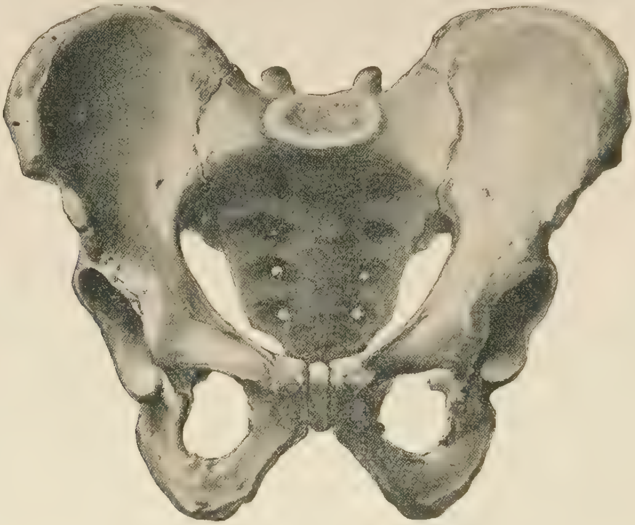


Fig. 4.—Male pelvis (slightly less than one-third natural size). (From the American Text-Book of Obstetrics.)

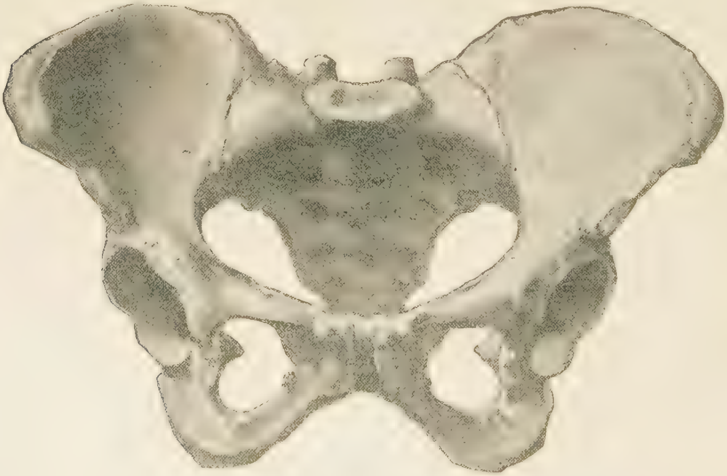


Fig. 5.—Female pelvis (one-third natural size). (From the American Text-Book of Obstetrics.)

is flatter and broader; the depth of the symphysis pubis is less; the subpubic arch is much wider and the space between the tuberosities of the ischia greater."

Race.—As far as the determination of race from a study of the body or bones is concerned, the investigator should be guarded in his conclusions. If the point be important, a competent anthropologist should be called as consultant. To one skilled in this phase of examination "The racial characteristics of the living or recently dead body are readily determinable from an examination of the skin, hair, and skull. When the skeleton alone is at one's disposal, craniometry may furnish the necessary data. The important features to be noted, in distinguishing skulls of different races are: (1) The cranial capacity; (2) the cranial length, breadth, height, and circumference; (3) the degree of projection of the jaws; and (4) the form of the nasal skeleton."

Stature.—The calculation of the stature is a simple matter if one has the entire skeleton with which to deal. Here the addition of 1½ to 2 inches to the measurement of the skeleton gives approximately the height of the original body. However, the determination of the stature becomes a much more complicated process and the errors are much greater when one has only isolated parts for study. If one can reconstruct a lateral half of the body by laying the bony structures in their approximate positions, then the measurements may be of the same relative value as mentioned above. In the absence of more definite data, certain rules, faulty at best, may be of some slight service in obtaining an approximate estimate as to stature. Thus, twice the length of the bones of the arm plus 12 inches for the clavicles and 1½ inches for the sternum gives the approximate height of the body; the length of the forearm from the tip of the olecranon process to the tip of the middle finger is said to be 5⁄19 of the height of the body. These are, of course, only general figures and can not be taken as representing anything more than an approximation.

Hair.—The examination of the hair may, very often, prove of great value in the identification of both living and dead. As hair resists the process of decomposition and putrefaction for a long period, it offers proof of identity when many other elements have been destroyed. It is clear that in the course of a struggle hairs may become detached from the head of either the assailed or the assailant and be found, in the one case, in the hands of the dead person, or, in the case of the latter, on his clothing or on the instrument supposed to have been employed. The determination of the fact that the suspected material is hair and that it has the same texture and color as that either of the deceased or the suspect often proves invaluable in the solution of crime.

The hair consists of a shaft, a root, and a bulbous extremity embodied in the hair follicle. Microscopically, the hair shaft consists of an outer cuticular fibrous portion and an inner medullary darker portion. The shaft is crossed by transverse lines due to the layer of flat cuticular cells that cover its surface. These imbricated scales are more permanent at the root of the hair. The fibrous portion of the shaft is composed of a very compact mass of fine fibrils. The medulla consists of spheroid cells containing air-bubbles, which, by transmitted light, appear as dark

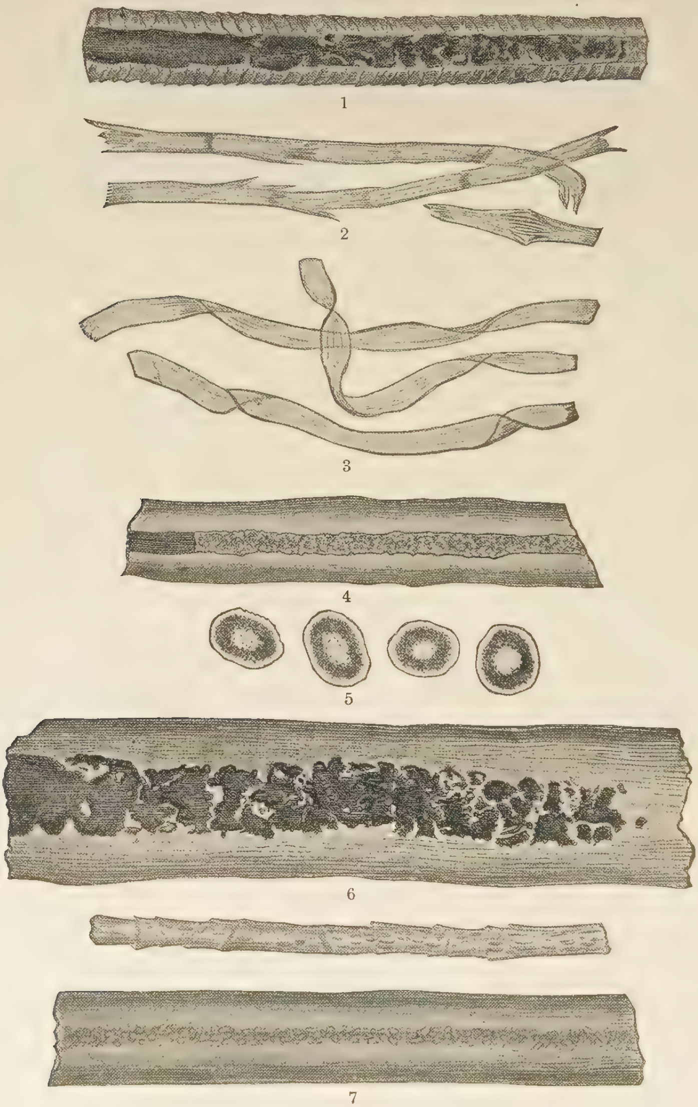


Fig. 6.—1, Sheep's wool (× 200). 2, Linen fibers (× 200). 3, Cotton fibers (× 200.) 4, Hair from human head (× 200). 5, Transverse sections of hairs from human head (× 200). 6, Hair from human beard (× 200). 7, Hairs from back of hand (× 200.) (From Belfield in Peterson, Haines and Webster, "Legal Medicine and Toxicology.")

granules. The medullary portion is absent from the very fine hairs of the general body surface, from the colored hair of the scalp, and from the hair of young children. Human hair differs from that of the lower animals in having more delicate and more numerous cross striations. The region of the body from which the hair has been removed can be determined with considerable accuracy from the length, size, color, stiffness, curliness, and general gross appearance. (Ewing.)

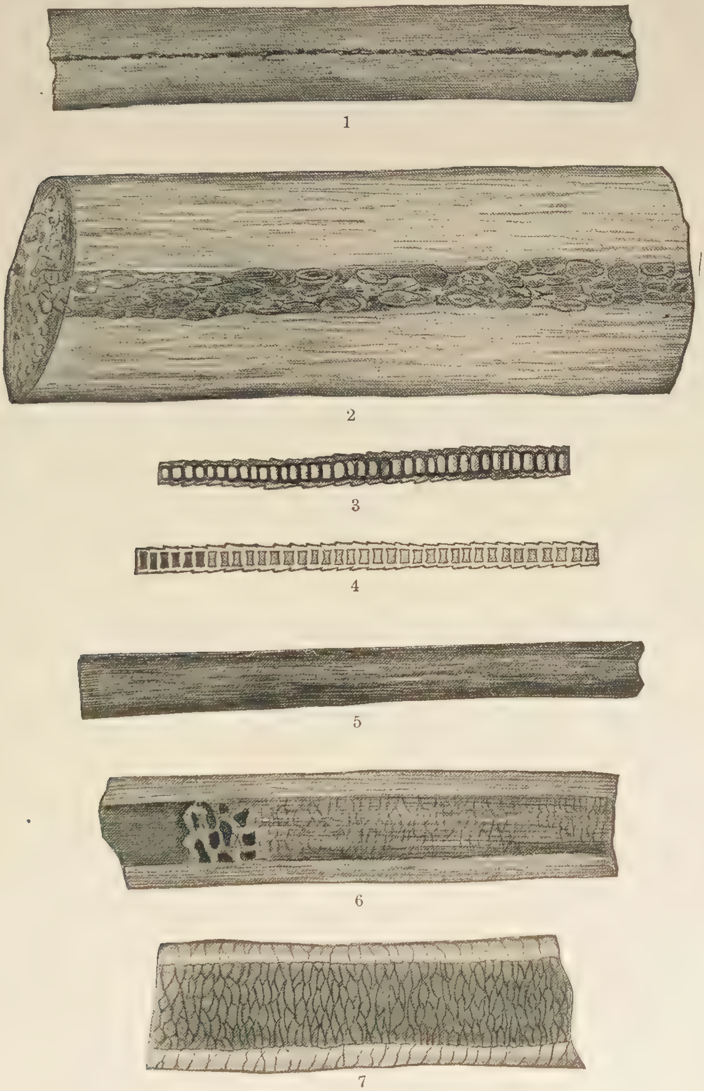


Fig. 7.—1, Hair of ox (× 200). 2, Pig's bristle (× 200). 3, Cat's hair (× 200). 4, Mouse's hair (200). 5, Horse's hair (× 200). 6, Donkey's hair (× 200). 7, Goat's hair (× 200). (From Belfield in Peterson, Haines and Webster, "Legal Medicine and Toxicology.")

Changes in the natural color of the hair occur from disease, from fright or shock, or from premature grayness of which the cause is unknown. Artificial coloring or bleaching of the hair is not infrequently resorted to by many individuals, but what is especially important is that criminals adopt this practice to cover up their identity. It must be remembered, therefore, that the color of the hair or the type of cutting it may have been changed and that too much importance must not be attached to the description of the hair as given in the records of the individual.

Teeth.—Peculiarities in the number, formation, and condition of the teeth are among the most reliable aids in identification. While such peculiarities may have been remedied or changed, yet some distinguishing marks may usually remain. The dentist is usually in a position to tell from his records just what was the condition of the teeth in a certain person, whom he may have treated, and is able to recognize his own work. The finding of artificial teeth and of a gold plate in the furnace ashes was a very strong point in the establishment of certain remains as those of Dr. Parkman, as the dentist positively identified the teeth as some that he had made for the missing man. It is, perhaps, wise in all important cases to make a cast of the mouth in order that one may be in a position to establish the condition of the jaw, the absence of teeth, their irregularities, and the presence of any dental work that may have been done.

CHAPTER IV

DEATH IN ITS MEDICOLEGAL RELATIONS

"Death may be defined as the cessation of those physical and chemical processes on which the phenomena of life depend." Death must, therefore, be related to the primary cessation of function of the vital centers, the heart, lungs, and brain. When the function of one of these centers becomes involved and ceases to act, the others also soon cease to function. Death, in the usual acceptation of the term has reference to the death of the individual, or *somatic* death, in contradistinction to *molecular* death, or death of the tissues. This latter type is going on constantly during the active processes of life, as the wear and tear of existence is necessarily associated with the breaking down and building up of our tissues, and it may continue for some time after somatic death as is shown by muscular irritability, the growth of hair and of nails after true somatic death.

CONDITIONS SIMULATING DEATH

There are, it is true, certain conditions which are characterized by a temporary inhibition of these vital functions, the appearances produced simulating closely those of true death. It is this fact that has lead many to fear that burial may take place before actual death, an hypothesis which does not appear to be tenable. However, that such conditions of suspended animation do exist should be borne in mind, so that every effort may be made to resuscitate those apparently dead.

Syncope.—This is the ordinary fainting attack, characterized by failure of respiration and circulation, coma and pallor, but is soon replaced by distinct signs of life. The fault here is primarily circulatory, the heart sounds being almost lost and the pulse almost undetectable. Although a not uncommon occurrence, yet it is always a dangerous condition indicating a temporary heart weakness which may rapidly pass into permanent cardiac cessation. It calls, therefore, for prompt measures to restore the circulation. One of the most remarkable cases reported is that of Colonel Townshend described by Cheyne.[1] Apparently Townshend had the ability voluntarily to suspend the action of his heart to such an extent that 3 physicians could detect no pulse nor feel any beating of the heart nor find any evidence of breathing, a condition which was maintained for about $\frac{1}{2}$ hour, when the physicians believed him to be dead. However, at the end of this time, they observed a slight movement of the body and were soon able to show that the heart and lungs had once more resumed their functions. This experiment by the physicians was made in the morning and Townshend really died that evening.

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[1] *English Malady: Or a Treatise on Nervous Diseases*, 5th ed., 1735, p. 307.

Partial Asphyxia.—This is a not infrequent cause of apparent death. Attempts at resuscitation of the drowning are said to have been successful when begun as long as one hour after submersion, so that measures should certainly be adopted to restore the circulatory and respiratory activities even in such apparently hopeless cases. Infants may be asphyxiated during a prolonged stage of labor or by pressure of the cord and may be revived several minutes after both pulse and respirations have ceased. However, as Loomis remarks, these are the exceptional cases and it is setting at defiance physiological experiences to suppose that the heart action and respiration, when once established, may be entirely suspended for such a long period. Loomis is lead, therefore, to state that if no motion of the heart occurs during a period of five minutes, death may be regarded as certain.

Catalepsy.—This is characterized by complete loss of consciousness of sudden onset. The muscles of the whole or a part of the body become rigid, the legs and arms being capable of movement and of being placed in different positions where they remain. The superficial reflexes are abolished, sensibility to touch and pain may be lost and the body temperature may be lowered. The respiration and heart's action are much reduced, although careful search will reveal evidences of feeble action. The muscles are, however, responsive to stimuli and no sign of rigor mortis appears.

Trance.—This condition resembles true death more closely than does catalepsy and has, in some instances, ended in death. The face is extremely pale. The limbs usually remain flaccid, but may become rigid or show spasmodic movements. Reflexes may be lost. Pupils are dilated and immobile. Sensation, although frequently retained or heightened, may be abolished. Pulse and respiration may become almost imperceptible. Muscles, however, show persistent excitability to electrical stimuli.

SIGNS OF DEATH

From the above discussion it will be evident that the answer to the question as to whether or not death has really occurred may require very careful study. As the physician is the one called upon to pass on this point, he must be in a position to make use of every possible sign as an indication of either life or death.

I. Cessation of the Circulation.—Obviously the most reliable method of determining the presence of cardiac activity is careful, prolonged, and repeated auscultation with the stethoscope, all distracting noises being eliminated as much as possible. While usually trustworthy, the results of this examination may not always be entirely convincing. As Ewing points out, "in very corpulent persons the normal heart sounds may be rather indistinct because of the thickening of the chest wall. Some pathological conditions may increase the natural difficulties of the case. In chronic interstitial or fatty myocarditis the heart sounds are usually feeble and may be indistinct. With pericardial effusions the heart sounds may be very obscure; while cases of transposition of the viscera or of displacement of the heart from chronic inflammation of the lungs are occasionally encountered."

When the stethoscopic examination is uncertain, resort may be made to tests for the presence of peripheral circulation. It is evident that the radial or carotid pulse may not be perceptible even though the heart is still beating. Should large parietal thrombi form during the latter moments of life, the peripheral circulation may be markedly disturbed and no amount of cardiac activity will avail to restore the circulation. Certain tests, other than the search for the pulse, have been advanced for determining this peripheral circulation, some of which offer, at least, corroborative evidence.

1. *Magnus' Test.*—If a ligature be applied to a finger or to a lobe of the ear, so as to cut off the venous circulation without disturbing the arterial current, the distal area will gradually become engorged with blood, the color becoming first reddish and then bluish and a white bloodless zone will form at the point of the ligature, providing the circulation has not entirely ceased.

2. If pressure be applied to the finger-nail, the nail becomes white as long as pressure is continued but, on releasing the pressure, again becomes pinkish if circulation still exists.

3. *Diaphanous Test.*—If the hand of a living person, with the fingers in contact, be held before a strong light it almost invariably appears reddish, while after death it is usually opaque.

4. *Cloquet's Needle Test.*—If a bright needle be inserted deeply into the body of the biceps muscle and allowed to remain for about 10 seconds, it will be tarnished (oxidized) on withdrawal if the circulation still persists.

5. If a drop of melted sealing wax, or other counterirritant, be applied to the forearm of a living person, redness or vesication occurs at the point of contact.

The absence of reaction to these tests within five minutes after supposed death will almost invariably indicate that death has occurred.

II. Cessation of Respiration.—The respiratory function is less able to withstand unfavorable conditions than is the heart's action, so that we usually find the respiration ceasing before the heart has ceased to beat, although occasionally the respiration may continue for a short time after the heart has stopped. If the respiration ceases suddenly while the action of the heart is unimpaired, the resulting asphyxia (apnoea) is marked by great venous congestion; but, if the asphyxia be gradual, due probably to the overcharging of the blood with carbon dioxide, the patient may die with pallor.

The possibility of restoring the respiratory action depends upon the vital condition of the respiratory center and the extent to which it has been depressed by the accumulations of carbon dioxide in the blood and tissues. As a rule the respiration can not be shut off for more than a very few minutes, without causing death. In rare instances, says Ewing, usually after long training, the breath has been held for four or five minutes, a period which will ordinarily suffice to render most persons unconscious. Death has repeatedly occurred after submersion in water for five minutes, although resuscitation has been successful after the body has lain in water one hour.

The procedures, which may be used to determine the question of final respiratory cessation are the following:

1. Careful and prolonged auscultation may be made over the chest, trachea, and larynx, but very feeble respiratory movements may produce no appreciable sound. This test is, however, probably the most reliable one.

2. Placing a cold hand-mirror before the mouth or nostrils, when the warm moist air exhaled will condense upon the mirror if respiration still persists. This test is of marked corroborative value but is not invariably reliable as is evidenced by the case of Colonel Townshend mentioned above in which the test failed.

3. A light downy feather or a few fibers of cotton placed over the mouth or nostrils will show slight movement if currents of air are being exhaled.

4. Winslow's test. If a saucer full of water be placed on the chest, slight surface rippling of the water will be observed if any respiratory movements are present.

III. Changes in the Eye.—The conjunctiva becomes insensitive and a thin film of mucus usually gathers over the cornea, which loses its luster and becomes glazed in appearance. Each of these conditions, according to Ewing, may be observed in the living and the latter is not an invariable accompaniment of death. It is stated by Guy and Ferrier that the eyes may continue brilliant and prominent for a long time after death from apoplexy, and from poisoning by carbonic acid and prussic acid, but Glaister, from examination of a large number of bodies where death was due to the first two of these causes, could not corroborate the conclusions. The iris is flaccid and the pupil moderately dilated and irresponsive to strong light, although solutions of atropine or eserine may, according to Tidy, alter the size of the pupil for about $\frac{1}{2}$ hour after death. Ophthalmoscopic examination may offer some points of interest. Poncet states that the anemia of the fundus after death is evident in the yellowish-white color which replaces the yellowish-red of the living condition; while Gayet asserts that after death the vessels of the fundus are completely emptied in the optic disk, and for some distance about it, while in the remainder of the fundus the vessels remain filled with blood. Bouchet regards pneumatosis of the veins of the fundus as a reliable and immediate sign of death.

IV. Cadaveric Changes.—"While none of the signs, as outlined above, can of itself be regarded as a conclusive proof of death, it cannot be admitted at the present day that in the hands of a competent person the complete examination of the body, even with reference to these so-called 'inconclusive signs', can ever lead to a false diagnosis of death. Yet none of the phenomena thus far considered gives any indication of the length of time that life has been extinct. The presence of *cadaveric changes*, however, is conclusive proof of the reality of death, and the sequence of these changes furnishes important evidence as to the time of death."

1. *Loss of Animal Heat.*—During life the temperature of the body is maintained at about 98°F. independently of that of the surrounding medium. At the time of death a slight rise in temperature may be observed, due to the failure of circulation and to excessive metabolic tissue changes which still continue. Indeed, post-mortem elevation of temperature of quite an extensive amount has been observed in such diseases as cholera, yellow-fever, small-pox, tetanus, rheumatism, etc. However, such rises are exceptional and the temperature of the body soon declines and progresses at a varying rate until it has reached that of the surrounding medium.

The time of cooling of the body is affected especially by the physical condition of the body, by the medium with which it is surrounded, and by the nature of the death. Thus, fat bodies retain heat longer than lean ones; bodies of adults cool more slowly than those of children or of the aged; clothed bodies cool more slowly than naked ones; bodies in water cool more rapidly than those in air; after chronic and wasting diseases the cooling is relatively rapid; after acute diseases or sudden death the process is slow; while after death by lightning or by suffocation the body may retain its heat for a considerable period.

The rate of cooling of the body varies from time to time, being more rapid soon after death and becoming slower as the body temperature approaches that of the surrounding medium. Thus, Goodhardt finds the rate during the first three hours after death to be 3.5°F. in the robust and 4.5°F. in the emaciated; during the second three hours 3°F. in both; and about 1°F. an hour thereafter until cooling is complete. Generally speaking the time necessary for a body to cool to the temperature of the air is from 15 to 20 hours, although Casper gives this figure as from 8 to 12 hours. As the actual time of cooling of any specific body will depend on the factors above mentioned, it is obvious that it is almost impossible to determine accurately the time of death from observations on the temperature of a corpse. Each case must be considered with the attendant circumstances and conditions in mind. The most recent attempt to arrive at an approximate determination of the time of death from a consideration of the rate of cooling is that of Vaughan[1], who divides the lower extremity into ten parts and allows one hour for the cooling of each division.

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[1] Jour. Amer. Med. Assoc., 1921, 76, 608.

2. *Changes in the Muscular System.*—The muscular tissues of the dead body pass through, as a rule, three distinct stages between the period of somatic death and that of molecular death.

(*a*) *Primary Flaccidity.*—In most cases death is followed by general relaxation of the entire muscular system for a period varying from five to six hours. In this state the muscles are flaccid and are responsive to mechanical and, especially, to electrical stimuli. Spasmodic muscular states present antemortem usually relax, although there is an exception to the rule in the spasmodic contraction (instantaneous rigor) of the muscles under the influence of very strong will power in cases of sudden or violent death. Such contractions are seen in the firmly clenched hand holding a revolver tightly clasped some time after death and, also, in the contracted hand of the drowned person firmly gripping bits of sand, grass, or weeds. In connection with the post-mortem response of muscle to electric stimuli it must be remembered that single muscles or groups of muscles lose their power of response before death, so that failure of such response must be regarded cautiously, as the cause and manner of death may effect the persistence of muscular irritability.

(*b*) *Rigor Mortis.*—The above period of muscular relaxation and contractility is followed by one of marked muscular rigidity. This cadaveric rigidity is due to the conversion of the myosinogen of the muscle into myosin under the action of a ferment and the coagulation of the myosin by the weak acids (especially sarcolactic acid) which are no longer removed from the system. In this state the muscles are very rigid and contracted, are distinctly acid in reaction and appear opaque.

The rigidity in this condition is very marked, the entire body being stiffened into a unified mass. If attempts are made to raise the leg of a body at a time when rigor mortis is complete, the result is the lifting of the entire body. If a stiffened joint be forcibly flexed, the mobility which results remains permanently, thus differing from the cataleptic rigidity in which flexion is followed by return to the former rigid state.

Rigor mortis occurs first in the involuntary muscles, the cardiac muscle being affected within an hour in most cases. Following this the voluntary muscles are affected in the following order: First the muscles of the eyelids; then the muscles of the lower jaw and neck; then the chest and upper extremities; followed by those of the abdomen and lower extremities. The disappearance of rigor mortis follows the order of its onset, those muscles first affected being those from which the rigidity first disappears.

The time of appearance of the cadaveric rigidity, following the primary flaccidity, varies greatly, but it may be stated that it appears generally within 5 or 6 hours and disappears in from 24 to 36 hours. However, there are marked exceptions to this rule, some cases showing almost immediate rigidity and others a delay in appearance as long as 16 hours; while the bodies of decapitated individuals may remain rigid for 8 or more days and, according to Kussmaul, bodies of muscular individuals dying suddenly may show this rigidity for two weeks or longer. Once the process of rigor mortis begins, it is usually complete in 1 to 2 hours.

A slow onset and long duration may be expected where death has occurred in a person of full muscular vigor; and, conversely, the more feeble or exhausted the muscular condition the more rapid the time of onset and the shorter its duration. Thus, in apoplexy or in death following injuries to the brain or medulla, a slow onset and long duration would be expected, death from hemorrhage being the most common cause of delayed rigor.

A rapid onset is shown in conditions marked by great muscular exhaustion, as after death from long-continued fevers, pulmonary tuberculosis, cholera, and poisoning by strychnine. Indeed, almost instantaneous rigor mortis may appear after sudden death during violent muscular exertion, as is evidenced by the many instances of soldiers, who have died under circumstances of severe muscular strain and who have been found set in the position present when they were killed. This sudden rigor may account for the cases of retention of a weapon or of a poison vial in the hands of a dead individual or of sand, grass, etc. found in the hands of drowned persons. Such evidence is often invaluable in throwing light on the question of suicide or homicide or upon the manner of death. The spasms of strychnine poisoning or of tetanus may pass directly into rigor mortis with no apparent interval.

(*c*) *Secondary Flaccidity.*—After a variable period of cadaveric rigidity, the muscles again become flaccid and movable, the flaccidity appearing in the same order as the rigidity. The muscles, in this state of final molecular death, are non-responsive to stimuli of any type and are alkaline in reaction.

3. *Cadaveric Lividities.*—After death the skin of the body has a peculiar ashy-gray pallor. Sometimes within an hour, frequently within six hours, and usually within twelve hours characteristic discolorations appear in the skin over dependent parts of the body. These are due to the distention of the capillaries with blood, which has flown to the most dependent parts under the influence of gravity. These lividities appear as livid patches of bluish or purple color on the back of the trunk, posterior part of head and neck, extensor surface of arms and flexor surface of legs. They do not occur upon those parts of the body which are in actual contact with the surface on which the body lies, as the capillaries have been emptied by this pressure, and the marks of clothing or constricting bands are indicated by bloodless streaks. Such hypostases or suggillations occur not only in the skin but, also, in the dependent portions of the internal viscera, and hence must not be mistaken for evidences of inflammatory processes. These discolorations increase until cooling of the body is complete. At a later period the color deepens due to the diffusion of blood pigment into the tissues surrounding the capillaries.

These post-mortem hypostases may, and have been, mistaken for ante-mortem ecchymoses produced by violence of some type. As a rule the ecchymotic areas are somewhat elevated although this is not invariable; post-mortem lividities are never raised. On section of the colored area only a few bleeding points will be observed in a cadaveric lividity, while in an ecchymosis either coagulated or fluid blood will be found extravasated into the tissues.

4. *Putrefactive Changes.*—The putrefactive processes occurring in the body after death are largely the result of chemical processes brought about by the ever present bacteria under the influence of a favorable temperature, free access of air, and the presence of moisture. Naturally, variation in these factors will change the course and rate of putrefaction. Donaldson[1] calls attention to the fact that there is a period elapsing between death and the onset of putrefactive changes during which pathogenic organisms, that may have established themselves in the blood, may be recovered in culture, if suitable precautions are taken. Such bacteriologic examinations may yield information of considerable medicolegal importance concerning the cause of death.

At a period varying from a few hours to three days a greenish discoloration is observed in the skin of the abdominal region. This coloration gradually deepens and, later, becomes purple or brown, due to the disintegration of the hemoglobin and the little understood action of the products of decomposition upon this altered blood pigment. This discoloration extends till the whole body is uniformly discolored at about the end of the second week. While the above external evidences of decomposition are appearing, gaseous products have been forming in the gastrointestinal tract, serous cavities, blood vessels, and internal organs, so that we have a marked distention of the cavities and tissues of the body. The skin becomes tense and elastic, and the features are swollen and soon become unrecognizable. The specific gravity of the body is reduced, so that bodies lying under water usually rise to the surface. The further steps in this process of decomposition result in the gradual disintegration of the body, the details of which may be found in the larger works of Legal Medicine.

In a considerable proportion of bodies buried in moist earth or submerged in water, the course of decomposition and destruction of tissue will be interrupted by the formation in the tissues of a whitish, solid, soapy substance, called *adipocere.* The formation of adipocere represents a true saponification of the fat contained in the tissues. This formation requires essentially a tissue containing fat, and the setting free of fatty acids, and an albuminous tissue, which, by putrefaction, develops ammonia (Ewing).

In bodies which are buried in shallow graves in the sandy soil of hot countries, the processes of decomposition may be interfered with to such an extent that the body dries up or becomes desiccated (mummified).

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[1] Jour. State Med., 1928, 36, 497.

This process is, however, a very infrequent one under ordinary conditions of burial. But, if the body be embalmed, especially by both the intravenous and cavity methods, the tissues may be found in excellent preservation for months and years, and after the lapse of considerable time may be completely mummified. However, many of the embalming fluids may not be reliable and the method employed may be unsatisfactory, so that many bodies, which are presumably embalmed, do not differ much in their decomposition processes from those above mentioned, the state of preservation being far from that desired.

THE CAUSES OF DEATH

All deaths were attributed by Bichat to one of three causes: (1) Death beginning at the heart, syncope; (2) death beginning at the lungs, asphyxia; and (3) death beginning at the brain, coma. While it is possibly true that many deaths may be directly traceable to involvement of one or the other of these vital centers, yet the functions of each are dependent upon the integrity of the other, so that impairment of the one is followed by functional disturbances of the others. As Ewing remarks "Death is, however, rather infrequently the result of an exclusive affection of the circulatory, the respiratory, or the nervous system, and it seems much more logical at the present day to discuss the causes of death in connection with the viscera principally involved in the lesion. Yet even such a scheme can necessarily serve only a temporary purpose, for the continued investigation of organic disease is constantly enlarging and readjusting ideas as to the relative importance of the various visceral lesions associated in these diseases. In the present state of the knowledge of pathology, one rests content when some morphologic change in the structure of a viscus, which it is the custom to call a *fatal* lesion, is discovered. Of the links in the chain which connects this lesion with the cessation of the complex process of life one is for the most part in ignorance, and the inability to point out the essential relation between change of structure and alteration of function in a cell or viscus renders it often a matter of conjecture to decide what constitutes a fatal lesion or which of many lesions is the essential cause of death. For instance, sclerotic kidneys are sometimes found at autopsy as an unimportant and secondary lesion in persons dying without renal symptoms, although this lesion, under many circumstances, would be at once accepted as the cause of death. Yet in neither case would the mere presence of connective tissue in the kidney give an explanation of the death of the patient. Even more difficult is the problem when dealing with cases of death from some poisons which leave no morphologic evidence yet demonstrated of their fatal action. So that it must be confessed that in some cases it is impossible to find any trace of the manner or cause of death, and in other cases to demonstrate any necessarily fatal result of existing lesions. Such considerations may serve to indicate the wide gap that exists in the knowledge of the relation of structural changes in viscera and the phenomena of life, and until this gap has been bridged over no final plan of classification of the causes of death can be constructed. Nevertheless it will not be well to retain a scheme which recognizes only the crudest notions of symptomatology and ignores the present knowledge of the essential pathologic basis of disease."

Sudden death arises from a variety of natural causes, of which disturbances of the heart, brain and lungs are the chief. However, many such deaths, especially in our larger cities, result from violence or poisoning, of which the exact cause can be determined only by a close study of the pathologic conditions in the body and, in cases of poisoning, by a very careful chemical examination of the viscera. Where the victim of sudden death has been under observation of a physician for some time, the symptomatology of the case may point clearly to the pathologic basis, but, oftentimes, nothing is known of the previous history of the case and, indeed, there may have been no warning that the possibility of sudden death was present. Many cases of sudden death, therefore, would certainly not have been considered as sudden had the history been available.

It is obviously impossible in the limited scope of this work to discuss in detail the causes of death and, especially, of sudden death, as the mere mention of the various pathological lesions, which may be regarded as causative, would be too extensive. We must, therefore, be content with reference especially to the discussion of this subject by Ewing[1] as covering the points involved in an extremely satisfactory manner.

Post-mortem Examination.—As pointed out above, to determine the exact cause of death it is necessary that a close and accurate study of the pathology of the various viscera, as revealed by necropsy, be made, and, even then, the cause of death may not be discovered. In cases of poisoning, for instance, the post-mortem findings are rarely anything more than significant, as few poisons produce characteristic lesions, so that all that may be determined in such cases is that the findings are compatible with poisoning from certain substances. It is to be recalled, in this connection, that if the physician desires to hold an autopsy upon the body of his patient in order to arrive at the exact cause of death, he must obtain the consent of the nearest relative before proceeding.

It was mentioned in our introduction that, in any case of violent or sudden death, or of death from unknown or suspicious causes, the physician may not be in a position to state the exact cause of death and cannot, therefore, sign the death certificate accurately. Under such conditions, the physician should report the case to the coroner or medical examiner, who will conduct an investigation, of which an integral part is an autopsy.[2]

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[1] "Sudden Death" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, I, 209.

[2] See "The Autopsy" by Karsner, Jour. Amer. Med. Assoc., 1927, **88**, 1367. Also, Warwick, Amer. Jour. Med. Sci., 1928, **176**, 536.

MARGIN RESERVED FOR BINDING

If a child is dead at birth this form must not be used—use original blue Stillbirth Form V. S. No. 7.
If the child lived any time after birth, even a single minute, it is not a Stillbirth and this original white form
V. S. No. 4 must be used.

WRITE PLAINLY, WITH UNFADING INK—THIS IS A PERMANENT RECORD

N. B.—Every item of information should be carefully supplied. AGE should be stated EXACTLY. PHYSICIANS should state CAUSE OF DEATH in plain terms, so that it may be properly classified. Exact statement of OCCUPATION is very important.

(82526–5M Bks.-2-12-23)

V. S. 4

☞ Has decedent ever served in military or naval service of U. S.?..................

STATE OF ILLINOIS **ORIGINAL**

Department of Public Health—Division of Vital Statistics

STANDARD CERTIFICATE OF DEATH

1. PLACE OF DEATH

Registration Dist. No.........................

County of..

(Show on line below the name of place where death occurred; give either City (or Village) or Township (or Road District), not both.)

Township, or Road District, or Village, or City, of..

Primary Dist. No......................

Registered No.................................. (Consecutive No.)

Street and Number, No.......................................St.; ....Ward, ...Hospital.

(If death occurred in hospital or institution, give its name instead of street and number)

2. FULL NAME..

Residence No........................., ...St.; ....Ward, ...

(Usual place of abode) (If non-resident give city or town and State)

Length of residence in city or town where death occurred yrs. mos. ds. How long in U. S. if of foreign birth? yrs. mos. ds.

PERSONAL AND STATISTICAL PATICULARS

3. SEX

4. COLOR OR RACE

5. SINGLE, MARRIED, WIDOWED, OR DIVORCED (Write the word)

5a. If married, widowed or divorced HUSBAND of (or) WIFE of

6. DATE OF BIRTH

...., 1........ (Month) (Day) (Year)

7. AGE Years Months Days If LESS than 1 day........hrs. OR.........min.?

8. OCCUPATION OF DECEASED

(a) Trade, profession, or particular kind of work..

(b) General nature of industry, business, or establishment in which employed (or employer)..

(c) Name of employer..

9. BIRTHPLACE (city or town)..

(State or Country)..

PARENTS

10. NAME OF FATHER

11. BIRTHPLACE OF FATHER

(city or town)..

(State or Country)..

12. MAIDEN NAME OF MOTHER

13. BIRTHPLACE OF MOTHER

(city or town)..

(State or Country)..

14. INFORMANT..

Address..

15. Filed........................., 192...... .... Registrar.

(P. O. Address)..Ills.

MEDICAL CERTIFICATE OF DEATH

16. DATE OF DEATH

...., 19.......... (Month) (Day) (Year)

17. I HEREBY CERTIFY, That I attended deceased from

..............................., 19.........., to..............................., 19..........

that I last saw h........ alive on..............................., 19..........,

and that death occurred, on the date stated above, at

..........m. The CAUSE OF DEATH* was as follows:

....

....

....

....(Duration) ....yrs. ....mos. ....ds.

Contributory (Secondary)..

....(Duration) ....yrs. ....mos. ....ds.

18. WHERE WAS DISEASE CONTRACTED

If not at place of death?..

Did an operation precede death?..........Date of..........................

Was there an autopsy?..

What test confirmed diagnosis?..

(Signed).., M. D.

Address..

Date.., 19.......... Telephone..................

*N. B.—State the disease causing death. All cases of death from "Violence, casualty, or any undue means" must be referred to the coroner. See Section 10, Coroner's Act. (See reverse side.)

19. PLACE OF BURIAL OR REMOVAL

21. DATE OF BURIAL

...., 19........

20. UNDERTAKER

ADDRESS

REVISED UNITED STATES STANDARD CERTIFICATE OF DEATH

Approved by U. S. Census and American Public Health Association

Statement of occupation.—Precise statement of occupation, is very important, so that the relative healthfulness of various pursuits can be known. The question applies to each and every person, irrespective of age. For many occupations a single word or term on the first line will be sufficient, eg., *Farmer*, or *Planter*, *Physician*, *Compositor*, *Architect*, *Locomotive engineer*, *Civil engineer*, *Stationary fireman*, etc. But in many cases, especially in industrial employments, it is necessary to know (a) the kind of work and also (b) the nature of the business or industry, and therefore an additional line is provided for the latter statement; it should be used only when needed. As examples: (a) *Spinner*, (b) *Cotton mill;* (a) *Salesman*, (b) *Grocery;* (a) *Foreman*, (b) *Automobile factory.* The material worked on may form part of the second statement. Never return "laborer," "Foreman," "Manager," "Dealer," etc., without more precise specification, as *Day laborer*, *Farm laborer*, *Laborer—Coal Mine*, etc. Women at home, who are engaged in the duties of the household only (not paid *Housekeepers* who receive definite salary), may be entered as *Housewife*, *Housework*, or *At home*, and children, not gainfully employed, as *At school*, or *At home*. Care should be taken to report specifically the occupations of persons engaged in domestic service for wages, as *Servant*, *Cook*, *Housemaid*, etc. If the occupation has been changed or given up on account of the DISEASE CAUSING DEATH, state occupation at beginning of illness. If retired from business, that fact may be indicated thus: *Farmer (retired 6 yrs.)*. For persons that have no occupation whatever write *None.*

Statement of cause of death.—Name first, the DISEASE CAUSING DEATH (the primary affection with respect to time and causation), using always the same accepted term for the same disease. Examples: *Cerebrospinal fever* (the only definite synonym is "Epidemic cerebrospinal meningitis); *Diphtheria* (avoid use of "Croup"); *Typhoid fever* (never report "Typhoid pneumonia"); *Lobar pneumonia; Bronchopneumonia* ("Pneumonia," unqualified, is indefinite); *Tuberculosis of lungs, meninges, peritonaeum*, etc., *Carcinoma, Sarcoma*, etc., of.................(name origin; "Cancer" is less definite; avoid use of "Tumor" for malignant neoplasms); *Measles; Whooping cough; Chronic valvular heart disease; Chronic interstitial nephritis*, etc. The contributory (secondary or intercurrent) affection need not be stated unless important. Example: *Measles* (disease causing death, 29 *ds.; Bronchopneumonia (secondary)*, 10 *ds*.. Never report mere symptoms or terminal conditions, such as "Asthenia," "Anaemia," (merely symptomatic), "Atrophy," "Collapse," "Coma," "Convulsions," "Debility" ("Congenital," "Senile," etc.), "Dropsy," "Exhaustion," "Heart failure," "Hæmorrhage," "Inanition," "Marasmus," "Old age," "Shock," "Uræmia," "Weakness," etc., when a definite disease can be ascertained as the cause. Always qualify all diseases resulting from childbirth or miscarriage, as "PUERPERAL *septicemia*," "PUERPERAL *peritonitis*," etc. State cause for which surgical operation was undertaken. (Recommendations on statement of cause of death approved by Committee on Nomenclature of the American Medical Association.)

All deaths from "violence, casualty, or any undue means" must be referred to the coroner; A MEDICAL CERTIFICATE OF DEATH IN SUCH CASES DOES NOT COMPLY WITH THE REGISTRATION LAW OF ILLINOIS. See Section 10, Coroner's Act.

The following list of indefinite terms will not be accepted as cause of death unless explained:

Abscess—Locate and describe.
Accident—Refer to Coroner.
Albuminuria—Disease causing?
Angina—Was it scarlet fever or diphtheria?
Ascites—Disease causing?
Asphyxia—Accidental, suicidal—cause?
Asthenia—State cause.
Atrophy — Cause of — tuberculosis, syphilis?
Auto {infection / intoxication} Cause of?
Bowel trouble—Name disease; diarrhoea, dysentery, enteritis, strangulation?
Blood poisoning—State cause.
Bottle feeding—What disease resulted?
Breaking down—What disease?
Cachexia—Cancer, syphilis, tuberculosis, malarial?
Cancer—Primary location.
Cardiac {Asthenia / Debility / Failure / Weakness} Not accepted.
Collapse—From what?
Cold—Not accepted.
Childbirth – Physiological — what caused death?

Cellulitis—Give location and cause.
Coma—Cause {alcoholic? / opium, etc.?
Convulsions—Cause {epileptic—puerperal? / children, diarrhoea-enteritis?
Cramps—State cause of.
Cyanosis—Cause of.
Decline—State cause of.
Debility—From what disease?
Delirium {alcoholic? / traumatic?
Dentition—Disease causing death?
Dropsy—Name disease causing.
Dyspepsia—What organic disease?
Eclampsia—State cause of convulsions.
Emphysema—State cause.
Exhaustion—State cause of.
External Violence—Refer to Coroner.
Failure of vital powers—What disease?
Feebleness—What disease?
Gastritis—State cause of.
Heart failure—See cardiac.
Hemorrhage—What part. and cause?
Inanition—Cause of?
Insolation (under 24 hours) (Coroner)?
Jaundice—Disease causing?
Malnutrition—Cause of?

Marasmus—What disease?
Milk infection {diarrhoea? / enteritis?
Miscarriage—State cause of.
Nervous {exhaustion / fever / shock} State disease.
Old age—What disease?
Operation—State part and disease.
Paresis—General paralysis of the insane, or not?
Peritonitis—Cause of?
Pernicious anemia {malarial? / tuberculosis? / syphilis, etc.?
Pneumonia {Broncho? {Primary or / Secondary / to what?} / Lobar?
Pyaemia—Cause of?
Salpingitis—Cause of?
Septicaemia—Cause of?
Shock—From what?
Surgical {operation / shock} State disease.
Syncope—State cause of.
Tetanus—State cause of.
Toxemia—State cause of.
Uremia—Acute or chronic nephritis.
Weakness—What disease?

As to the technic of performing these medicolegal postmortem examinations, we shall have nothing to say, as we prefer to refer for such details to the articles of Hektoen and Le Count[1] and of Loomis[2].

CERTIFICATION OF DEATH

As stated in the Chapter on "Obligations of Physicians", every physician is required by law to report the exact cause (primary and secondary) of death of any of his patients. In doing this he must state the *disease* causing death and not symptoms or terminal conditions. It is, of course, of the greatest importance that this certificate be accurately and completely filled out. As Wood[3] points out, "In the matter of inheritance and other legal matters, the family of the deceased deserve protection by a correct certificate. The public has a right to the help rendered from a statistical compilation of the death records." In this connection we give, as covering the matter in a more detailed form then a discussion, a copy of the death certificate now in use in many of the States and in which is the United States Standard Certificate of Death approved by the U. S. Census and American Public Health Association.

LEGAL STATUS OF THE DEAD BODY

There is no right of property, in the ordinary sense of the word, in a dead human body; but for the health and protection of society it is a rule of the common law, which has been confirmed by statutes in all civilized states and countries, that public duties are imposed upon public officers, and private duties upon the husband or wife and the next of kin of the deceased, to protect the body of the dead from violation and see that it is properly interred, and to protect it after interment.[4] The law casts the duty of burial of the wife upon the husband and of the husband upon the wife. But if the deceased dies intestate, leaving no husband or wife, the duty of burial is cast upon the next of kin, in the order of right to administration. Where the deceased leaves a will appointing executors, these executors have a right to the possession of the body, and the duty of burial is imposed upon them. Generally, the estate of a decedent should be charged with the expenses of burial, and it is not an infrequent provision of last wills and testaments, that such expenses are directed to be paid before any division of the estate is made.

Where the right of burial has been exercised, and the body interred, no person has any right to interfere with it without the consent of the owner of the grave, or of the properly constituted public authorities.

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[1] "The Technic of Medicolegal Postmortem Examination" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 78.

[2] "Medicolegal Autopsies" in *Medical Jurisprudence, Forensic Medicine and Toxicology*, by Witthaus and Becker, 1906, **I**, 833.

[3] Jour. Amer. Med. Assoc., 1928, **90**, 1534. See, also, "Report of the Committee on the Accuracy of Certified Causes of Death" Amer. Jour. Pub. Health, 1928, **18**, 565.

[4] See Becker in *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 1906, **1**, 779, from which section this discussion is largely excerpted.

A dead body belongs to no one and is, therefore, under the protection of the public. If it lies in consecrated ground, ecclesiastical authorities will protect it, but whether in ground consecrated or unconsecrated, indignities offered to the remains, or the act of indecently disinterring them, are the ground of an indictment. Even the purchaser of land upon which is located a burial ground may be enjoined from removing bodies therefrom, if he attempts to do so against the wishes of the relatives or next of kin of the deceased. Every interment is the concession of a privilege which cannot be repudiated. On the other hand, the right of the municipal or state authorities to remove dead bodies from cemeteries with the consent of the owner of the burial lot or in the execution of the *right of eminent domain* is settled. After the right of burial has once been exercised by the person charged with the duty of burial, no right to the corpse remains except to protect it from unlawful interference.

Where a body has been buried, and the coroner believes that an inquest is necessary, he has power to disinter the body and hold his inquest, and he may direct a necropsy to be made, but after having done so he must cause the body to be reinterred. Practically all of the States have statutes to the effect that the unlawful removal of bodies from the grave or aiding in such removal, or, in some cases, having in possession a body so removed is punishable as a felony. It must be remembered that the performing of an unauthorized autopsy on the body of a dead subject is uniformly recognized as a violation of the right of property which the nearest of kin has in the corpse.

Most of our states carry in their statutes provisions directing that dead bodies of those required to be buried at public expense shall be turned over, by the officers in whose custody such bodies are held, to the medical colleges of the state or to physicians or surgeons for medical study, providing due notice of death has been given to relatives or guardians of the deceased, unless the deceased requested to be buried or the body is claimed for burial by the next of kin.

PRESUMPTION OF DEATH

The question of probable death often arises in the case of an individual not heard of for a long period of time. "It is contrary to the tendency of modern law that the courts should recognize any *presumption* in matters of fact which, if the facts were known, could be determined with certainty." Naturally, presumption of death must depend upon general evidence, the question involved being a presumption of a fact that must be determined by a jury. If, however, a person remains absent and unheard of for a period of seven years from the time he was last seen or heard from, he is presumed to be legally dead.

Questions of presumptive death may arise in the settlement of estates, adjustment of life insurance, remarriage of a wife or husband, etc. In such cases it is not always regarded as necessary to wait the full seven years before settling the affair, as there may have been strong evidence pointing to the great probability of the death of the individual. Thus, where a ship on which the person was known to have sailed has never been heard of or has been known to have been wrecked, the law may assume that the person in question was dead, although cases are known of return of the individual after he has been declared legally dead. However, in such cases direct proof of death may not be required, the law assuming that the presumption of death is logical and sufficient to warrant settlement of an estate, payment of life insurance, or remarriage of a wife, for instance. Further, such presumptions may be strengthened by such evidence as known threats of suicide, known ill health of the individual, enlistment in the army or navy in time of war, etc.

PRESUMPTION OF SURVIVORSHIP

It is a difficult and, oftentimes, very important matter for the courts to determine which of two or more persons is to be regarded as the survivor, when all perish in a common accident. "It is at once evident that the decision should be determined strictly by the facts of the case, for it can hardly be supposed that the deaths of two or more persons in the same catastrophe are exactly simultaneous, while the difference in the time of death however slight it may be, constitutes a real distinction. Yet the great variety of circumstances surrounding fatal accidents on sea and land and the usual lack of direct evidence as to the fate of the victims are usually insurmountable obstacles in the way of ascertaining these facts. Accordingly, the attitude of the law among civilized nations in treating the question of survivorship has been determined partly by ideas of expediancy and partly by consideration of the probable course of events." (Ewing.) The importance of such decisions rests, largely, on the fact that the transmission of inheritances may be adjusted along entirely unexpected lines, or even along lines which may not have been intended or desired by the deceased individuals. Although the law is slow in applying general rules of probability to individual cases, yet medical testimony is usually considered with care and its proper presentation involves the consideration of various conditions that may affect the length of life. Factors, which may be of some importance in relation to the question of the probable survivor, are as follows:

Age.—For this to play much of a rôle in the decision it is probably necessary that the persons be exposed to nearly identical conditions. If a father and a child under fifteen be exposed to the same conditions of violence, the presumption is in favor of the father. Between the ages of fifteen and sixty, there is no presumption, although men under fifty years of age may be far less vigorous than a boy of fifteen. Between a middle-aged man and one under fifteen or over sixty, the presumption is, obviously, in favor of the adult. Even in making these assumptions, however, the conditions involved must be considered. It is true that children are very susceptible to the fatal effects of shock, hemorrhage, starvation, and of some drugs, while the elderly are especially sensitive to both extreme heat and cold. In England the question has been recently settled by the passage of the Law of Property Act, so that disputes regarding survivorship there are reduced to a minimum. It is enacted by this law that in all cases where two or more persons have died in circumstances (such as shipwreck, battle, earthquake, or motor car collision) which render it uncertain which of them survived the other or others, such deaths shall (subject to any order of the Court) for all purposes affecting the title of property be presumed to have occurred in order of seniority, and, accordingly, the younger shall be deemed to have survived the elder.[1]

Sex.—There appears to be a presumption in favor of the male, when the loss of life is traceable to exhaustion of physical strength or when great courage is demanded. In any individual case, however, such presumption may be very wide of the actual condition, as the female may be much the stronger of the two. If it is a question of passive endurance and bearing of pain and hardship, then the presumption turns in favor of the female.

State of Health.—This may, of course, far outweigh any presumption in favor of either age or sex. An adult male, who is an invalid, will obviously have less chance of surviving the usual forms of violence than either a healthy adult female or a child. It seems reasonable, therefore, that the courts should listen carefully to the medical testimony as to the condition of the health of the parties involved in the case, providing any facts are available along these lines. That courts do, however, occasionally disregard the unimpeached testimony of experts upon such questions is shown by the case cited below.

Manner of Death.—This would seem to be the most important factor in permitting a conclusion as to the possible survivor in any given case.

1. *Asphyxia.*—In cases of death from breathing asphyxiating gases, it is generally considered that women consume less oxygen than men and that, therefore, the presumption of survivorship is in favor of the female. While certain series of cases studied in Paris would seem to bear out this presumption, yet other factors may play a much more important rôle, as, for instance, the proximity of each of the individuals to free air and the relative exposure of each to the higher concentrations of the poisonous gas. Moreover, as has been said, "Observations in such cases, to be reliable, must include the minutest details of age, habits, state of health, and especially of the position of the bodies with reference to possible sources of air." The case of Pehl et al *v.* Butt et al[2] is very interesting in this connection, as it is one of the few recorded cases in which the question of survivorship after exposure to fatal quantities of carbon monoxide has been adjudicated.

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[1] See Smith, *Forensic Medicine,* 2nd ed., 1928, p. 42.

[2] Northwestern Reporter, 1923, **193**, 988 et seq.

In this case the court of Green County, Wisconsin, under Judge Sherron found "That there is an absence of proof tending to show: (*a*) Which one of the four, to wit, Henry Butt, his wife, Ernestine Butt, Henry Butt Jr., and Harold Butt, his two sons, died first; (*b*) which of the four survived the others; (*c*) the actual survivorship of Henry Butt and the members of his family." The Court here failed to give due weight to the unimpeached testimony of expert witnesses, who were shown to possess expert knowledge of carbon monoxide poisoning as may be seen from a perusal of the facts, as stated in the decision of the Supreme Court of Wisconsin, which reversed the finding of the lower court.

On the night of November 23, 1920, five persons, sleeping in a room 7½ feet wide, 16 feet long, and 8 feet high, met their death by monoxide gas poisoning. The tragedy was not discovered for several days thereafter. When found, Henry Butt was lying on his back near the south wall at the back of the bed. The ceiling sloped down toward his head, conforming to the roof. His wife, Ernestine, lay on her back at the front of the bed. She held at her right side, with his head pillowed on her shoulder, her youngest son, two years old. A second son, three years old, lay on his right side facing the father and between the father and mother. The bed stood in the southeast corner of the room near the walls. The south wall was the only outside wall. A brother of Mrs. Butt lay on the mattress on the floor. There were two windows in the room, but both were tightly closed, and the door leading into the room was also tightly closed. There was a hot air furnace burning hard coal in the basement. Whether the gas came through the hot air register located near the center of the north wall just above the base board, or whether it found its way through cracks in the door, is not definitely disclosed. In the record it is rather assumed to have come through the register. The father and mother were each 23 years of age. There is some dispute as to their relative condition of health, but we may assume for the purposes of this case that they were both in fair physical condition. The children were robust and healthy. These facts are undisputed, and the question before the court was as to survivorship. The testimony worthy of consideration, aside from that of the undisputed facts, came from experts. The appellants introduced Dr. Warren Hill, Dr. Henry G. W. Reinhart, and Dr. E. R. Le Count, each of whom had had considerable experience in cases of carbon monoxide poisoning. Each of these witnesses testified in substance that, assuming the conditions heretofore stated, it was his belief, based on his experience and knowledge of monoxide gas poisoning and the effect thereof upon the human system, that the father was the first victim of the poisoning, and that the mother and the children survived the father. They reached this conclusion chiefly from the fact that women, living an indoor life, become more or less immune to the toxic effects of gas, and, also, that they require less oxygen than men, who live an outdoor life. As to the children, these witnesses testified that young children require less oxygen than older people and that, under similar conditions of gas poisoning, they would outlive the father in this case, but might not outlive the mother. They, further, testified that, owing to the size and shape of the room, of the cold outside wall, and warm inside walls, the point of entry of hot air and gas, and the relative weight of carbon monoxide gas and air, a current of air would exist in the room, which would carry the gas to the father first, and that he would thus receive the first and stronger volume of gas. On the part of the defense two physicians were produced, Dr. Lloyd H. Helms and Dr. R. R. Clark, neither of whom had had any special experience with carbon monoxide poisoning. Both of these witnesses testified that there was nothing in the evidence or in their experience that would permit a conclusion as to which of the decedents died first or which of the family survived. There was nothing in their testimony that impeached, in any way, the evidence of the witnesses for the appellant. In rendering the reversal decision, the Supreme Court, Judge Crownhart giving the decision, stated as follows: "As we view this case, the evidence is practically undisputed and only one conclusion can be drawn, if we are to give the expert evidence any weight, and that is that the children and the mother survived the father. That the children survived the father, all the expert evidence is in agreement. The trial court evidently disregarded the expert testimony, following the rule often laid down that such evidence is to be viewed with caution and may be disregarded altogether where it conflicts with the common knowledge of the judge and jury. However, there is a class of expert testimony that is competent, worthy of consideration, and which cannot be ignored by the trial court or jury, and that is the evidence of those persons, who by reason of special study and experience possess knowledge and judgment not possessed by mankind in general. Where expert testimony is properly admitted, it must be weighed and considered as other testimony. In this case there were many physical facts which the judge might consider together with the expert testimony. But without expert testimony the cause would have been left wholly in the dark. It was only by respondents' expert witness that the cause of death was determined. The size of the room in which the deaths occurred, the location of the entry of the poisoned gas, the location of the bed and the position of the bodies thereon, the age of the decedents, together with their physical condition, were physical facts established in this case. But the effects of monoxide gas on different persons when inhaled, its relative weight and its diffusion with the air, the probable currents of air following the heat that came from the hot air register, were properly matters of expert testimony. None but experts could know the effect of monoxide gas on the human system or how it would affect different persons under different circumstances. We consider that the trial judge was bound by such expert testimony in the absence of anything to impeach it. The evidence being substantially all one way, the duty of the court was to find accordingly. The judgment of the county court is reversed, with directions to enter judgment in favor of the appellants."

2. *Drowning.*—Here the question is complicated, as one must take into account the age, sex, relative strength, and opportunity of each for safety. Men being stronger, more often able to swim, less encumbered by clothing, and more apt to be on deck at the time of the accident, have the best chance for safety, but, in case of accidents at sea, the women are first taken care of in the boats, so that a woman, although she may be drowned later by the capsizing of the small boat, may, nevertheless, survive her husband who has remained on the ocean liner. If both are thrown into the water at the same time, then the presumptions mentioned above may be given some weight, although courts have repeatedly refused to place any great value upon such general presumptive evidence. In case of two or more persons, all males, equally exposed, no presumption can be entertained unless it can be shown that one or more of the individuals could not swim, were weak or sickly, or lacked much self-possession, or, should the bodies be recovered, marks of bodily injuries be found on some of the persons, which would, obviously, interfere with their efforts to save themselves.

3. *Cold.*—Men endure cold better than women, and adults better than the aged, while children are least capable of withstanding its effects. As a general rule, the greater the body weight, the longer will life be retained, as the excess adipose tissue serves as protection to a certain extent. So, also, the person with the most suitable clothing will resist the cold the longer. Excessive use of alcohol or of narcotics will lower the power of resistance to cold.

4. *Parturition.*—"It is probable that in most cases of parturition ending fatally to mother and child, either with or without attendance, the child perishes before the mother, but the conditions in the case may distinctly indicate that the chld survived the mother." Should the mother die of hemorrhage after the child is born, the chances of the survival of the child are quite favorable. However the decisions of the courts are usually in favor of the survival of the mother, on the ground that the life of the child requires proof, while that of the mother does not. The decision of this question is often of the greatest importance, as inheritance may depend on the birth of a child, which survives the mother.

CHAPTER V

DEATH FROM ASPHYXIA

Definition.—By the term *asphyxia* is meant the fatal or deleterious result of any interference with the normal processes of respiration.[1] The process of asphyxiation may be technically understood to include any interference with the passage of properly oxygenated air along the respiratory tracts, the prevention of the lungs from receiving such air, and any interference with the proper power of the blood to combine with and convey oxygen and carbon dioxide to or from the tissues. For medicolegal purposes asphyxia includes the general results of mechanical interference with the passage of air to and from the lungs and the prevention of the respiratory interchange between the pulmonary alveoli and the blood.

"Within the limits of such a definition, death from asphyxia may be considered as embracing death from strangulation, death from choking, and death from suffocation, including intoxication by certain deleterious gases. By the term *strangulation,* as here used, is meant to be understood the interference of the passage of air to the lungs by external compressing force applied to the throat or neck, as in hanging or throttling. *Choking* should be understood as applying to those cases in which interference with respiration has resulted from obstructing agencies within the air-passages, such as foreign bodies, false membranes, strictures or tumors of the air-passages, or the presence of neutral or irritating gases or fluids interrupting the movement of the respiratory air to or from the lungs mechanically or by producing spasmodic constriction of the walls. The term *suffocation* may be employed to include all mechanical influences applied externally elsewhere than about the throat in the prevention of respiration; and may, for convenience, be required to include the results of those agents which, through their toxic influence upon the blood, render it unfit for convection of the respiratory gases. In this sense suffocation would be properly applied in such cases in which the mouth and nostrils are closed by some external substance, as a pillow or a mass of mud (often spoken of as *smothering);* where the respiratory movements are prevented by the presence of a crowd or of a weight upon the chest; or where, as in poisoning by carbon monoxide gas, the hemoglobin of the red blood-cells is no longer able to enter into combination with the oxygen of the air or carbon dioxide of the tissues.

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[1] See section on "Death from Asphyxia" by Smith and Lucke in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2,** 351, from which much of this discussion is taken.

Moreover, here should be classified the rare cases of respiratory prevention from rarefaction of the surrounding atmosphere and confinement in a close space."

General Symptoms of Asphyxiation.—The term *asphyxia* literally means pulselessness or lack of pulse, so that as applied to interference with respiration the term is undoubtedly misused. Some would prefer the term *apnea* as this means lack of respiration, but the former term has acquired the authority of usage for so long that it is difficult to replace it.

Asphyxiation may be gradual, as in death from various diseases, or may be sudden, as in some diseases or in accidental or intentional interference with the respiration. If the respiratory failure be gradual we may note "a general sense of discomfort, muscular weakness, nausea, headache, profuse perspiration, lividity of surface, rapid or slow weak pulse, labored respiration, loss of consciousness, development of anesthesia, death." If the respiration is suddenly shut off, there may be a brief period of quiet followed by more or less violent efforts to obtain air, these movements ceasing within four or five minutes and unconsciousness and insensibility follow; finally all respiratory movements cease but the heart continues to beat for a few minutes thereafter. The face, and especially the lips, becomes cyanosed, the eyes are prominent and the pupils dilated; there is a feeling of fulness in the head, roaring in the ears and memory of past events is said to crowd in upon the mind. Occasionally the interference with respiration is so marked that death is almost instantaneous. Just how long will be required to produce death in any given case will depend upon the age and constitution of the individual, the degree of oxygenation of the blood when asphyxia was imminent, and the extent of the interference with the respiration. Death from asphyxia is, in reality, due to an excess of carbon dioxide in the blood and the tissues. Interference with proper respiration and hence proper aeration of the blood allows carbon dioxide to accumulate. This leads to constriction of the arterioles and, secondarily, to increased cardiac action. By reflex action the respiratory center is first stimulated to increased action and, finally, as the carbon dioxide accumulates, the center becomes exhausted and respirations cease.

Post-mortem Appearances.—Usually there is lividity of the surface of the body, especially of the face, lips, ears, and nails (especially noticed in children). The face may be distorted and frothy mucus may come from the mouth and nostrils; the eyes are open and staring, the pupils dilated, and the conjunctivae congested; and the tongue may be in its normal position or partly protruded, depending upon the type of asphyxia.

On internal examination the lungs are found to be engorged with dark blood, marginal emphysema may be present, and small endothelial ecchymoses (Tardieu spots) may be found on the surface of the lungs especially in children. The right side of the heart is engorged with dark uncoagulated blood, as are also the venae cavae; while the left cavities of the heart are empty. The brain and abdominal viscera are found engorged and, occasionally, there are small patches of hemorrhage in different situations from the excessive passive engorgement. As Smith and Lucke remark "In the examination of a body dead from asphyxiation, in addition to the recognition of the general mode of death, constant and great care is to be exercised in the discovery of such evidence as may be given by the body and the surroundings upon the particular mode of production; and the coexistence of pathologic conditions capable of causing death naturally by asphyxia and the careful estimation of their importance and influence are questions certain to arise in any legal proceedings upon the subject."

I. DEATH BY STRANGULATION

"Death by strangulation is the fatal result of compression of the fauces, larynx, or trachea by any forces externally applied to the neck. This form of producing asphyxiation includes those cases where throttling by the hand and compression by some encircling band about the neck, as the garrote of the Spanish, the bowstring of the Turks, or a cord or cloth as used by the thugs of India, have been the methods of destruction, as well as hanging, where, the neck being partially or completely encircled by a band suspended from a superior fixed point, the weight of the victim's body is in more or less suspension."

1. Death by Throttling.—Throttling by the hand is a common form of homicide and attempts at it are frequent in cases of robbery, assault and rape. Where strangulation by means of a constricting band is attempted it is usually homicidal in nature, although suicide by this method is fairly common. Further, accidental strangulation by constriction of the neck with a rope has occurred in children in play and excessively tight clothing has produced very serious effects; while pressure of a hard substance against the throat, as in cases where a person has fallen senseless with the throat across a board or rock, has proven fatal.

In throttling by the hand the assailant's hands grasp and compress the throat. If both hands are used, the marks of both thumbs may be on the same side of the victim's throat, or one on each side and a series of larger marks on the side opposite the thumb mark. It thus happens that the level of the external bruises will vary depending on the mode of applying the pressure.

If a constricting band be employed instead of the hand in producing the strangulation, the line of pressure of the ligature or band will take a more or less circular course around the neck, although there is usually some part of the course which is missing. Various agents have been used in this method of strangulation, some of them being especially characteristic of certain localities. The narrower the constricting band, the more evident is the line of pressure, while the broader the band the less the evidence of injury to the superficial structures.

The symptoms noted in this form of death by asphyxia are practically the same as those previously outlined. Here, of course, there are the violent muscular efforts of the victim attempting to free himself from his assailant. Loss of muscular power and consciousness are usually quite rapid, owing to the associated pressure on the large blood vessels and nerves in this form of homicide. Owing to the congestion in the head, hemorrhage from the nose and ears may be observed.

The post-mortem appearances in strangulation with a compressing force or by the hand are those previously mentioned. In this form of death the position of the tongue will depend upon the level of the neck that receives the force of compression and how the compression is directed. "If the compression is applied high up above the hyoid bone, the tongue is forced into the back part of the mouth. If the pressure be below the hyoid bone the tongue will protrude between the jaws unless the compression has a decidedly downward direction, when its position may be normal."

Specially to be noted are the marks of violence upon the throat of the victim. If the hands furnish the pressure, the marks on the throat show as dark bluish or brownish blotches corresponding to the outline of pressure. These appear at different levels on the two sides of the throat, the thumb mark being somewhat higher, as a rule, than the marks caused by the fingers.

On dissection of the tissues of the neck, more or less bruising and laceration of the tissues, fractures of the cartilages of the larynx and of the hyoid bone, even hemorrhage into the larynx may be noted. If the compression has been accomplished with a ligature, a line of depression corresponding in general to the width of the constricting band may be observed. This line of depression may be marked by ecchymoses and is usually horizontal about the neck. If the depression is very deep and there has been some laceration of the skin, the line of depression becomes dry, hard and more or less parchment-like some little time after death. The presence of signs of violence in other parts of the body than the neck is of importance in deciding as to the possibility of the death being homicidal or suicidal.

2. **Death by Hanging.**—This is a form of strangulation in which the body of the victim, more or less completely suspended by a ligature or cord which encircles the neck, exerts the constricting force by its own weight. The whole body need not be suspended, partial suspension being sufficient to produce death providing there is sufficient interference with the respiration. While the effect of the cord encircling the neck together with the constricting force of the weight of the body is to shut off the air passages and, hence, to prevent air entering the lungs, yet death is not always due to asphyxia in such cases as the stoppage of the cerebral circulation, due to pressure on the large blood vessels of the neck, may be sufficient to cause death. Also, there may be enough injury to the cervical cord or to the pneumogastric nerve to produce

death at once. While it must be granted that there may be cases of hanging in which the ligature is so adjusted that the respiration is not completely shut off and the compressing effect is exerted more upon the vessels and nerves, in which cases the usual signs of asphyxia will be absent; yet the majority of suicidal and all of homicidal and judicial hangings are associated with death from asphyxia because the suspending cord is so attached above the thyroid cartilage or the hyoid bone that the structures are jammed together, the epiglottis being pushed against the pharynx, the base of the tongue being pressed into the cavity of the pharynx so that the entrance of air is completely cut off.[1]

In *judicial hanging* the individual stands upon a trap-door in the floor of an elevated scaffold, the arms and legs are bound, sight is prevented by a cap over the face and the noose of a properly tested elastic rope is tightly knotted about the neck. The upper end of this rope is firmly attached above the head of the criminal and sufficient length is allowed for a drop of 5 or 6 feet, the length of this drop being in inverse relation to the weight of the victim. The noose of the rope is drawn fairly tight about the upper part of the neck and is so arranged that the knot comes below and behind one ear. Occasionally the knot is adjusted to the back of the neck or it may be placed anteriorly beneath the chin. After these preparations are made, the trap door is sprung and the body drops the length of the rope. If everything has been properly arranged, death may occur at once from injury to the spinal cord or medulla by dislocation of the vertebrae or fracture of the odontoid process of the axis, or death may be almost immediate from causes above mentioned. However, in the majority of cases death occurs from asphyxia or from asphyxia associated with some of the other possibilities and requires from eight to twenty minutes after the drop. It is to be remembered that death has not occurred until the heart ceases to beat, as resuscitation is possible after the respiration alone has stopped. "When death is immediate, the body, except for a few slight muscular quivers, hangs motionless, the head fallen over to the side opposite the knot and the neck looking as if it had been stretched." In the usual cases, the body hangs limp for a short time, then convulsive movements of various muscles take place, lasting for two or three minutes and then disappear. The respiration has then ceased but the heart continues to beat, gradually becoming more and more feeble until it stops at the end of ten to twenty minutes, when death actually occurs.

In *homicidal hanging* the effect is similarly performed, the drop being given by suddenly removing the support upon which the victim was standing. More often in lynching the victim is drawn up by the neck from the ground and held suspended until death occurs. In these cases the damage to the cervical structures is relatively slight as there is little or no fall and death occurs almost entirely from asphyxia.

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[1] See Zeitler, Ztschr. f. d. ges. ger. Med., 1928, **12**, 380.

Suicidal hanging may resemble either judicial or homicidal cases. The individual, having made his plans and adjusted the rope, may jump from a support or kick it from beneath him. In either case the drop is usually not great and the suspension may be only partial, the body being found with the feet touching the floor, or the body kneeling, or even only the head and neck suspended. As there is relatively little violence in such hangings, severe injuries to the cervical structures do not occur and death is the result of asphyxia, although fatal syncope may be the result.

Accidental hanging is rare and generally happens with children at play with ropes or swings. Occasionally a child may become suspended by the neck band of clothing to a projecting railing or may slip from a fence and catch its neck between the upper ends of the palings. In such cases the struggles of the child simply hasten the approach of asphyxia.

Many of the appearances noticed in hanging are subject to variation depending upon the type and degree of compression. Thus, while usually the face becomes cyanosed and swollen from interference with the venous circulation through the jugulars, a considerable proportion of cases present a pallid countenance. This is especially apt to be the case when death occurs quickly from causes other than asphyxia, such as those previously mentioned. So, also, if the adjustment of the loop and attachment of the ligature leaves one side of the neck free from compression, the unobstructed veins of the non-constricted side carry off the blood sufficiently rapidly to prevent cyanosis and congestion. "A pallid countenance can exist only where the venous circulation is, at least in part, free, or where there is absolutely no further access of blood by the deep and unobstructed arteries of the neck, as may be expected, for instance, when death has occurred from syncope." For the same reason, the protrusion of the eyeballs and the conjunctival congestion, so often noticed, may be absent. The tongue may be either normal in position or may be protruded between the teeth, although in some cases it appears rather retracted, depending on the position of the ligature and the line of traction. As a rule the face appears more or less contorted, although it is often quite placid. The hands may be tightly clenched or the fingers may be fully extended. The turgescence of the external genitals, and the discharge of genital fluid, urine and feces may be noted, but these are not peculiar to death by strangulation.

Post-mortem Appearances.—In inspecting the body of one dead from hanging, one should note carefully the surroundings and every possible feature that may have any bearing on the case, before the body is disturbed. Evidences of a struggle, marks on the body, the manner of attachment and the type of the ligature, the place of attachment of the knot, the probable length of the drop, and the degree of suspension, should all be noted. Likewise, the condition and color of the face, the state of the eyes, the color of the mouth, the position of the tongue, the contracted or relaxed condition of the muscles of the hands, arms and legs, the condition of the clothing, and any other salient points should be recorded. After the body has been freed from the suspension, the ligature removed and carefully examined, and the body is open for inspection, careful examination should be made of the marks upon the neck in order to permit of conclusions as to the homicidal or suicidal nature of the hanging or as to the possibility of the body having been suspended after death from some other cause had occurred.

Many differences may be noted in the character of the marks of the constricting cord. Usually there is a single line of depression, passing obliquely about the neck and most marked on the side opposite the knot and entirely absent close to the knot. This line follows, especially in suicidal hangings, the edges of the lower jaw and passes obliquely up behind the ears. When the position of the victim is such that the force of suspension does not act along the line of the axis of the body, the mark about the neck may be horizontal, as in strangulation with a cord, instead of oblique. However, unless a slip-knot has been used, Smith and Lucke believe that the absence of the mark on the side of the neck corresponding to the knot of the ligature forms an important means of differentiation of hanging from throttling. In suicidal hangings in which double or triple ligatures are used or the cord has been wrapped twice or more around the neck, there may be several lines of compression, one being horizontal and the others oblique. This possibility points to the necessity of carefully examining the ligature before studying the marks made by it. In general, the looser the adjustment of the loop, the more oblique the line of depression. The constricted line is deeper as a rule along the sides of the neck, the weight of the body, the length of the time of suspension, and the size and nature of the constricting cord being the chief factors in determining the depth. The narrower the constricting ligature, the deeper the furrow of depression. This furrow is pale at the bottom and the margins are swollen and discolored. Instead of pallor along the bottom of the depressed line, the surface may look normal or slightly red if the suspension has been brief and little force was used. When considerable force has been used, ecchymoses along the bottom of the groove may be noted, but probably not as frequently as in throttling. If there has been much excoriation by the ligature and the suspension has lasted for some time, the skin in the bottom of the furrow may have a yellowish-brown tint and a hard, dry appearance, the so-called "parchment skin." The upper margin of the groove is almost invariably cyanotic, while the lower margin is usually less cyanotic, or cyanosis may be absent. Ecchymoses along the margin of the groove are more common above the line than below.

Lacerations after hanging, especially where there has been considerable violence with the drop, are more or less frequent. The sternocleidomastoid muscle may be considerably lacerated and the inner coats of the carotid arteries torn. In some cases the hyoid bone is broken, the thyrohyoid ligament may be torn, or there may be dislocation of the thyroid, cricoid, and rarely of the arytenoid cartilages. Dislocations of vertebrae, occasionally associated with fractures are not uncommon, the most frequent example of this being the odontoid process of the axis or a dislocation of the axis from the third vertebra. The surrounding tissues are often the seat of hemorrhage and the membranes of the spinal cord or the cord itself may be severely lacerated.

The question not infrequently arises in cases of hanging as to whether it was suicidal or homicidal. Here the condition of the body and, especially, evidences of injuries other than those about the neck and which were probably not self-inflicted are of importance. Ordinarily homicidal hanging is much rarer than the suicidal type, as it is a very difficult process to carry out unless severe injury or even death has occurred prior to the hanging. If the body hangs freely and there are no agencies about from which the victim might have jumped or fallen or upon which he might have gotten up high enough to have adjusted the loop, the evidence is fairly clear that the case is one of homicide. On the other hand, the inference in cases of incomplete suspension is of suicide, the absence of other signs of violence on the body corroborating this view.

II. DEATH BY CHOKING

By this term is indicated all cases of fatal asphyxia resulting from the occlusion of the air-passages by agencies within these passages or their walls, such obstructions being either of external origin, solid, liquid or gaseous, or arising within the body as the result of disease. This latter type plays no role in medicolegal cases except from the standpoint of differentiation as to probable cause of the asphyxiation. The occlusion may be the result of a direct mechanical plugging or filling by the substance, or of a laryngeal spasm or spasm of the glottis induced by the irritation from the substance.

1. Choking by Solids.—Usually in choking by a solid mass the occurrence is accidental, although homicidal choking, by forcing substances into the back of the mouth or even into the glottis, is occasionally seen, especially in very young children, and suicidal choking is not infrequent with the insane. Accidental choking may occur from swallowing of too large and too hard a bolus of food, which, by causing compression of the posterior respiratory wall, may close the air-passages. Occasionally this bolus is too large to enter the upper part of the esophagus and overlies the epiglottis or the opening of the glottis, thus preventing inspiratory movement of the air. Or, smaller bits of food may get into the opening of the glottis and close it. Many small objects have been known thus to enter the upper respiratory tract and to pass downward, but these do not cause the severe immediate symptoms because the access of air is still possible.

One notes, as conditions especially prone to lead to choking, attempts to speak or swallow at the same time, crying out when some small foreign substance is in the mouth, and trying to inhale while partially vomited matter lies in the pharynx. Children are frequently subject to accidental choking, owing to their practice of placing various articles in the mouth.

Symptoms.—If occlusion occurs in swallowing or breathing, the subject is at once seized with distress and apprehension, the demand for breath being almost immediate and intense. He may grasp the throat with the hand, stretch out his neck, and "clear the throat" in an endeavor to dislodge the mass. He assumes all sorts of attitudes and makes many contortions and the most violent efforts at coughing are exerted. As in the other forms of asphyxiation, the face, at first pale, soon shows signs of agony and becomes deeply congested; the eyes become prominent; the mouth is open and the tongue often extended; saliva may drip from the mouth and a blood-tinged foam may appear at the lips; and the face and neck are bathed with perspiration. Vomiting and involuntary discharge of urine and feces may occur. In a short time, depending on the degree of occlusion and the vigorous nature of the subject, the victim becomes unconscious. While the marked respiratory efforts continue for a few minutes, they soon cease, and the pulse gradually diminishes in force and finally ceases several minutes after the respiration has stopped. "The dyspnea of partial occlusion is peculiarly slow when the obstructive substance is located at a high level, as in the trachea or larynx, but is characteristically rapid when the obstruction is located in the bronchial tubes, particularly in the smaller ones."

Post-mortem Appearances.—If death has been due to asphyxia, the findings previously mentioned will obtain, while if the death be due to syncope or cardiac inhibition such signs will not appear. Especially noted in death from choking are the appearances of the mucous membranes of the respiratory passages, which are usually hyperemic and show considerable mucous secretion, usually blood-tinged, over the surfaces. At the level of the occluding substance the membrane is red and swollen and may show marks of direct injury.

2. Death by Drowning.—Drowning is the fatal result of asphyxiation caused by complete or partial submersion of the victim in water or other liquid medium. Usually in drowning the body of the victim is surrounded by liquid, yet there are not infrequent cases in which only the mouth and nose of the victim are submerged in the liquid. Further, there are other cases of sudden death on submersion, in which the subject dies from syncope or shock with no submersion of the respiratory openings. These latter cases can, of course, not be regarded as due to drowning, as there are none of the elements of drowning present and death occurs before the respiration has been shut off by the submersion. This has been well expressed by Glaister[1] when he says it may be taken as a safe rule "That if a person falls into the water—the process of respiration being in operation or resumed in the water—and if he die therein, the proximate cause of death will be asphyxia, of which the signs will be apparent on examination of the body; but the measure of their intensity will be determined by the struggle for breath, and the time occupied in dying."

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[1] *Medical Jurisprudence and Toxicology*, 4th edition, 1921, p. 182.

Symptoms.—There are really two types of drowning, aside from the few cases in which death is due to syncope and, hence, can not properly be included in the list of actual drownings.

1. In the first group we find those cases, relatively few in number it is true, in which the asphyxia is primarily due to spasmodic closure of the glottis as a result of the irritation of the water entering the mouth and nose, or from nervous reflex to the sudden chilling of the external surface of the throat. In such cases little water actually enters the respiratory tract unless the submersion is prolonged when a small amount may enter. In such cases the victim usually sinks at once, rising possibly once, and then remains below the surface, unconsciousness coming on in a few seconds. After a few ineffective convulsive efforts the respiratory attempts cease, the heart stopping a few minutes later.

2. In the second group, in which asphyxia is the cause of death, are included most of the actual cases of drowning. Here the asphyxia is due to the actual entrance of water into the larynx, trachea, bronchi, and even the bronchioles. The individual, on being submerged, attempts to get to the surface in order to breathe, but when he does reach the surface his efforts are more or less convulsive and he is very likely, unless he be an experienced swimmer, to draw in a small amount of water with the air. His violent expulsive efforts, sputtering and coughing result in actually diminishing the air in the lungs rather than in increasing it, accelerates pulmonary congestion, and brings on non-aeration of the blood. In these efforts much water may enter the lungs, unless there is spasm of the glottis, and, in addition, more or less water will enter the stomach, and the victim rises and sinks several times in his efforts. The individual may grasp at any sort of support and even when on the bottom of the pond or other body of water, he may grasp weeds, mud etc., in his efforts to hold on to something. In this type of drowning, the face is usually cyanosed, after the first few minutes of the obstruction, the eyes are prominent, the features are contorted, and the respiratory efforts are excessive. After one or two, or at the most three or four, minutes respiration ceases, but the heart continues to beat for some minutes longer, gradually stopping in systole. This is the usual sequence of events in drowning, but as Woodman and Tidy[1] remark, "The mode of death may vary owing to drunkenness, or from striking the head against a rock, or post, or stone, or even against the water or mud at the bottom, which may cause fracture of the skull and concussion, or the blow may be felt in the chest or at the pit of the stomach, or some other part of

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[1] *Forensic Medicine and Toxicology*, 1877, p. 818.

the abdomen, when death may be due to shock; or there may be fright, as in hysteria, when death may result from syncope; or an epileptic fit may happen at the moment of striking the water; or there may be extravasations of blood or serum during the struggles, producing apoplexy; or death may happen from the heart, owing to the cold, or from spasm or paralysis of the muscles of respiration."

Post-mortem Appearances.—Rigor mortis is usually early in the drowned, especially when there have been violent struggles before death. The surface of the skin may be marked by "goose flesh" (*cutis anserina*), which may be regarded as evidence of submersion having taken place before molecular death has occured but, in itself, is not peculiar to death by drowning. The general surface of the body is usually pale, although there may be small patches of discoloration. The face may be either pale or livid, depending largely on the time the body has been submerged and upon type of death. Congestion of the conjunctivae may be noted. The mouth is usually open and the tongue may be in normal position or between the teeth. At the mouth or nostrils may be observed a fine foam or froth which is very suggestive of drowning. Glaister calls attention to a rosy hue of the lips and of the skin over the malar bones, which he has noted in several cases which have been drowned in winter or in intensely cold weather. The joints of the body may be somewhat flexed, the hands often holding objects with which they have come in contact. The skin of the hands and feet may show a peculiar livid, grayish-blue sodden condition, from the wrinkled, puckered nature of which it has been styled the "washer-woman's hand." In examining the hands, attention should be directed to the nature of the substances

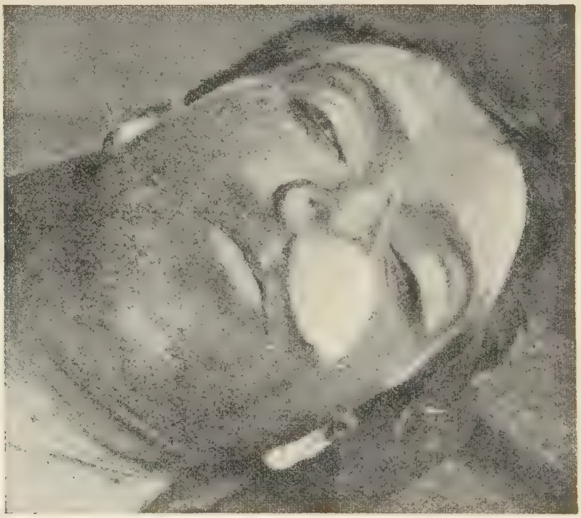

FIG. 8.—Drowning. Fine froth at the nose. (From Sydney Smith, "Forensic Medicine," J. and A. Churchill, London, Publishers.)

held and of the mud, sand and other debris under the nails. Contraction and retraction of the penis may be noted, although this is not a constant finding.

On autopsy the blood often oozes freely from the slightest cut. The right side of the heart is full of blood, while the left is small and empty and, as in other cases of asphyxia, the blood is found in the venous system and is dark and fluid. There may be a slight excess of fluid in the pericardial and pleural sacs. The lungs are increased in volume and "balloon" out on opening the thorax, the lung structure being firm, boggy and crepitant, usually hyperemic, the cut surface showing a copious, bloody, frothy fluid. In some cases, especially when death has happened immediately after submersion, the respiratory passages may show little else than a slight hyperemia of the mucous membrane. However, where gradual asphyxia has occurred, water is usually found, the amount not being over a few drams or ounces and being seen mostly in the trachea and larger bronchial tubes. Water as such may not be detected, but there is usually a fine, white, lather-like froth all through the bronchial system and in the trachea and larynx. This froth is a fine-bubbled one, is white in color and may persist for ten or twelve days after drowning if the body remains submerged. Its existence in large amount in the larger passages indicates that these passages were largely filled with fluid at the time of asphyxiation.

The abdominal organs are almost uniformly congested and dark in color. The stomach may contain more or less water, which has been swallowed during the drowning. If the body is thrown into the water after death, water, or at least very little, gets into the stomach. In this connection it must be remembered that water may have been drunk prior to the submersion, so that an error in interpretation might arise from this source. It is wise, therefore, to examine the stomach contents for evidence of foreign particles which are known to have been in the fluid in which the body was submerged. A sign of much importance in deciding the question of submersion either ante or post mortem is occasionally shown by aspiration of the middle air, as a small amount of water may be forced into this cavity during the struggles during drowning. As water does not enter this cavity after death, if it be found here submersion before death would be indicated.

As a reliable test for drowning and, also, for differentiating ante from postmortem submersion Gettler[1] advocates the determination of the chloride content of the right and left heart. The test depends upon the entrance of water into the lungs during drowning, which, by osmosis, dilutes the chloride content of the blood. Normally the chloride content of the blood in the right and left sides of the heart is about the same, the greatest difference being 5 mg. per 100 cc. of blood. In all cases of drowning examined by Gettler, the difference was always greater than

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[1] Jour. Amer. Med. Assoc., 1921, **77**, 1650; see, also, Yamakami, Tohoku Jour. Exp. Med., 1923, **4**, 88.

5 mg., ranging from 19 to 294 mg. When drowning took place in fresh water the left heart chamber always showed the lower chloride content, while in drowning in salt water the opposite occurred. The degree of difference depends upon the amount of water entering the lungs and on the time interval between the entrance of water and death. If the individual is thrown into the water after death, no water can get into the left heart. The method of examination of the blood should be learned from the original source or from works on Clinical Pathology.

Treatment.—Attempts to resuscitate those apparently dead from drowning are more successful with those becoming immediately unconscious when falling into the water (death being really due to syncope or shock) and with those in whom death occurs with little struggle and the asphyxia is due largely to spasm of the glottis. In cases of real drowning, in which the classic picture of asphyxia is present, it is probably true that there is little hope of resuscitation of one submerged for four to five minutes. When the mouth is so covered with water that air cannot enter the respiratory passages, asphyxia practically always comes on within one or two minutes, although the heart may continue to beat for some minutes longer. The ability of restoring the respiratory activity depends on the condition of the lungs at the time of removal of the body from the water as well as upon the time of submersion. Although the actual period at which asphyxia may be regarded as complete varies from one to four or five minutes, cases of resuscitation have been reported after various periods of submersion, such as 10, 13 and 20 minutes and Guérard[1] records a case which happened on Oct. 22, 1774 and in which resuscitation occurred after submersion for "about an hour" (dans lequel la submersion dura près d'une heure). This case is of rather doubtful authenticity, as it is probable, as Woodman and Tidy remark that "the evidence as to time is rather weak." It would appear fairly certain that where submersion has lasted for more than 4 to 5 minutes, there is usually little hope of success. However, the circumstances as to time are often uncertain, so that it is well to make the attempt on any body removed from the water, unless, of course, signs of putrefaction are evident and, also, it is wise to continue these efforts for quite some time before deciding that they are fruitless.

As soon as the body is recovered, it should be placed with the head and shoulders depressed and face downwards, the mouth open and the tongue drawn forward, in order to promote drainage if possible. All rough methods should be avoided. Artificial respiration should then be promptly resorted to, using preferably the Schäfer method in which the body lies face downward,[2] or, if one desires, the Sylvester method, in which the body rests on the back, continuing either method for ½ to 1 hour at least. Forcible traction of the tongue, synchronous with the inspiratory movements of the artificial respiration may be of distinct value. As soon as breathing is noticed, the wet clothing should be removed from the body, hot flannels and blankets should be applied to the body and hot water bottles to the feet, and cardiac stimulants administered by hypodermic methods. The pulmotor may be employed, if readily available, but time should not be lost in waiting for its arrival and, when used, it should be employed only by those accustomed to its use. Constant attention to the patient, after resuscitation, is required for several days in order to prevent sudden fatal syncope or other complication, which may occur in spite of all efforts.

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[1] Ann. d'Hyg. Pub., 1850, **44**, 306.

[2] See Drinker, "Acute Asphyxia as a Medical Problem", Jour. Amer. Med. Assoc., 1928, **90**, 1263. For the details of this Schäfer method see Treatment of Carbon Monoxide Poisoning.

Legal Considerations.—There are three questions which usually arise in connection with death from drowning: (*a*) Was death actually due to drowning, or was the body placed in the water after death from some other cause? (*b*) Was the drowning accidental, suicidal, or homicidal? And (*c*) How long has the body been in the water?

(*a*) Death by drowning may be stated with reasonable certainty if the following external and internal signs obtain: Face and surface pallid or discolored; froth of a peculiar, fine-bubbled, lathery character at the mouth or nostrils and in the larynx, trachea and larger bronchial tubes; water in the lungs, stomach and middle ear; diffuse and marked congestion of the lungs, abdominal viscera and brain; blood dark and fluid and present largely in the right heart and veins; presence in the firmly clenched hand of the victim of objects which are found in the water in which the body was submerged; contraction and retraction of the penis in the male. These signs may not all be present in one actually drowned, but the presence of the fine foam, the engorged condition of the lungs, and water in the stomach, as well as the signs of asphyxia to a more or less extent, will practically always be found. In a body thrown into water after death from other than drowning, the presence of the foam and water in the lungs would not be noted. Further, the body would show marks or signs of wounds that would be suspicious of other methods of death. If a body were strangled or hanged and then thrown into the water, the signs of asphyxia would, of course obtain, but it is not probable that water could enter the lungs and stomach after death.

(*b*) In determining whether drowning was accidental, suicidal, or homicidal, the main reliance must be placed on collateral evidence. If there are no signs of external violence on the drowned body, the case may reasonably be regarded as either accidental or suicidal, although certain evidence may point to the actual homicidal character of the case. Thus a person, even a very powerful one, might be pushed into the water and no signs of violence obtain. So, even if there are marks of violence, one should not be too quick in making his decision as suicides are prone to attempt to make things certain by such measures as shooting or stabbing themselves when in such a position that they would fall into the water after the injury. So, also, in suicidal death from jumping off bridges or other elevations, the body may strike some obstacle and be seriously injured and even killed before striking the water.

Homicidal drowning is much rarer than the suicidal form and is rarely free from signs of the violence necessarily employed. For the purpose of concealment of the actual method of crime, it is not infrequent for a criminal to throw a murdered body into the water. In such cases it is to be recalled that the signs of submersion above enumerated cannot be simulated by submersion after death. If such signs of actual drowning are present, the previous violence could have been only contributory to the death.

In accidental drowning there may or may not be signs of injury on the body of the victim. Such accidents occur in those working near the water, bathers, children falling into ponds or even into such common household articles as buckets, wash tubs, drunken individuals falling into rivers, creeks, etc., or even persons wandering into such places in the dark. It is often difficult to determine whether some of these cases are suicidal or accidental.

(*c*) It is almost impossible to state exactly the duration of submersion of a body. Whatever opinion one decides to offer, must depend upon the alterations in the body from maceration and putrefaction. Devergie[1] has outlined these changes in a general way based on his experience at the Paris morgue, but these statements are open to wide variation depending on such factors as season and climate and the consequent temperature of the water; depth of submersion; character of the water; motion of the water; and state of general health of the body at the time of submersion. Hence, it may be said that answers to the above question should be very guarded, consideration being taken of the fact that the signs of putrefaction in water appear, in general, only about half as fast as in air.

3. Death from Choking by Gaseous Matter.—The choking influences of gases manifest themselves in two ways, either by directly provoking a spasm of the glottis from irritation, or by mere exclusion of oxygen from the respiratory tract. The most common gas acting in such a manner is carbon dioxide. Marsh gas, nitrogen and hydrogen, by excluding oxygen, and such irritant gases as chlorine, bromine, ammonia, or the vapors of the mineral acids, and the irritant poisons used in the late war, by causing spasm of the glottis, may induce asphyxiation. The discussion of these gases will be given in their proper place in the sections on Toxicology.

III. DEATH BY SUFFOCATION

The term suffocation includes all cases in which air is prevented from entering the lungs, not by pressure applied externally to the windpipe, but by some mechanical cause which operates on the mouth or nostrils externally and upon the throat, or air passages internally. In this sense it covers some cases, which we have discussed under choking, as well as cases in which the obstruction may be due to pressure on the chest preventing respiratory movements and those in which the mouth may be covered by various substances, and, finally, those cases in which the asphyxiation is due to the toxic and mechanical effects of the irrespirable gases. It is clear, therefore, that suffocation may be due to accidental, suicidal or homicidal causes, as well as to natural diseases.

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[1] Ann. d'Hyg. Pub., vol. II, p. 160; vol. V, p. 429; vol. VI, p. 209. Quoted by Woodman and Tidy, *Forensic Medicine and Toxicology*, 1877, p. 825.

1. Suffocation from External Causes.—The most common method of homicidal suffocation is that known as "burking" so named from the famous murderer Burke, who, with his associate Hare, at first employed pitch plasters over the mouth to prevent breathing, and accomplished several murders by the following method: The victim is thrown to the ground and held down by the weight of the assailant's body upon the chest; the criminal holds the mouth and nose of the victim shut with one hand, while with the other, unless otherwise required by the struggles of the victim, he attempts to force the lower jaw up against the upper and thus to close effectually the respiratory openings. If the attempt is successful, death generally results in three or four minutes with all the symptoms of other forms of asphyxiation by external mechanical means. A similar means of suffocation or smothering is intentionally or unconsciously employed as a means of infanticide, the parent overlaying the child, thus preventing any attempts at crying and making respiratory movements impossible. The body of the parent here answers the same purpose as the hand in "burking", or clothes, bed clothing, or pillows may accomplish the same result. Smothering has occurred when individuals have fallen in an unconscious or helpless condition face downwards into mud, plaster, ashes, feathers, grain, etc., which occlude the mouth and nostrils. Further, instances of suffocation in crowds have happened in which the asphyxiating cause is the great pressure exerted upon the chest and abdomen of the victim.

2. Suffocation from Internal Causes.—In a general sense all lesions impairing the receptive power of the lungs as well as conditions preventing proper passage of oxygenated blood to the tissues and its later return to the lungs, may produce suffocation. These conditions are numerous and need not be enumerated. Aside from the above, the effects of gases, which prevent the proper respiratory exchange, are the most usual causes of internal suffocation. Such cases are frequently encountered by firemen working in burning buildings. With the toxic gases, much depends upon the type of gas as to whether or not there is asphyxiation or some specific action of the gas itself. As Henderson and Haggard[1] put it: "There are two types of asphyxia: (1) asphyxia caused by the cessation of breathing, and (2) asphyxia caused in some other way and without cessation of breathing, except as a terminal event. The distinction between these two types lies in the presence in the first of an excess of carbon dioxide in the body. The second consists wholly in deficiency in oxygen. The first of these forms of asphyxia occurs when breathing is stopped either mechanically or by action of a drug upon the respiratory center; the blood then fails to obtain oxygen from the air. This may be due to obstruction of the windpipe or other form of strangulation, or to drowning. It may result from the action of some drug such as morphine or chloroform, which causes a cessation of the respiratory movements. However it may be caused, there is not only a deprivation of oxygen, but an almost equally significant cessation of elimination of carbon dioxide. As the anoxemia develops the carbon dioxide also accumulates; and both conditions exert effects on the body. On the other hand, in asphyxia of the second type caused, for example, by the inhalation of a high concentration of nitrogen, the tissues of the body are primarily merely deprived of oxygen. In such asphyxiation the elimination of carbon dioxide is not interfered with; the anoxemia alone exerts a direct action on the body. As a secondary effect this form of asphyxia may even involve such excessive breathing that the content of carbon dioxide in the body is also greatly depleted. Thus to anoxemia is added acapnia. Asphyxia of the first type is the common cause of death from noxious gases which are not classified as asphyxiants, but which as part of their drug action abolish respiration. Asphyxia of the second type is the characteristic effect of the group of gases and vapors which are properly termed asphyxiants."

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[1] *Noxious Gases.* 1927, 96.

Among the irrespirable gases we may mention carbon monoxide, sulphuretted hydrogen, arseniuretted hydrogen, hydrocyanic acid, chlorine, and vapors of the anesthetics. These toxic substances are discussed in the section on Toxicology, to which the reader is referred.

Symptoms.—The course of events in all these varieties of suffocation from agencies operating externally, as well as those producing their effects internally (with the exception of specific toxic effects of certain gases), is similar to that discussed under strangulation, except that, in suffocation the compression of the vessels and nerves of the neck and the violence to the tissues of the neck and spinal cord do not occur.

Postmortem Appearances.—These are practically those already discussed under other forms of asphyxiation. As a general rule, however, the more rapid and complete the process of asphyxiation, the more distinct the external lividity. When the victim has been smothered by the application of the hand over the mouth and nose, local signs of violence may appear. Smith and Lucke call special attention to the finding of rupture of the tympanic membrane in many cases of this type of asphyxia. In cases where the individual is smothered by falling into or being buried in sand, ashes, feathers, grain, etc., as a rule the obstructing material will be found in the mouth, nostrils, esophagus, stomach, or larynx, unless the suffocating mass is not sufficiently light to enter readily these structures. When suffocation has resulted from compression of the chest and abdomen, examination will usually reveal local injuries, either superficial or deep.

CHAPTER VI

DEATH FROM COLD, HEAT, AND STARVATION

Both cold and heat may produce fatal effects when applied to the animal body under proper conditions, the method of action in each case being very similar. These untoward influences may be considered as partly exerted upon the circulatory apparatus and function, and partly, especially in the case of the action of heat, to the influence of toxic products formed in the body by irregular metabolism and discharged into the blood. Just how these influences are induced is not known, but it is probable that the action on the vasomotor centers, the vessels themselves and the cardiac ganglia is brought about either directly or through nervous reflexes or by the toxins mentioned. "These toxins, of whose actual nature definite information is yet to be had, are partly those which are naturally generated by the animal body and retained by reason of the impotency of surface excretion, partly the result of local degeneration of tissue influenced by the cold and heat, and partly the result of a general functional derangement induced by the abnormal temperatures of the body and vascular derangements consequent to the same."[1]

DEATH FROM COLD

Although a moderate degree of cold has an invigorating effect on a person, yet exposure for long periods may produce untoward effects. Hence, the degree of cold required to produce death will vary widely in different individuals, depending upon the power of heat production and upon the measures to prevent heat dissipation in these individuals. For this reason we find that some persons react very strongly to relatively mild temperatures, while others, under proper conditions, withstand very low temperatures without any marked effects. Of course one must admit that the action of cold is much more evident in those worn out physically or nervously exhausted, in those at either extreme of life, or with those who are addicted to the use of alcoholics. Women seem to stand cold better than men, owing to the influence of a greater deposit of subcutaneous fat. Persons who eat mostly a vegetable diet are less likely to withstand cold than those who eat freely of meats and fats. The influence of clothing in the maintenance of the body temperature is great, as it prevents rapid heat dissipation. In this connection it is clear that several layers of clothing are much more efficient in maintaining different strata of warm air between the skin and the external air than when the same weight is applied in one layer.

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[1] See "Death from Cold, Heat, and Starvation" by Smith and Lucke in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, I, 234.

Symptoms.—In ordinary cases of exposure to cold, the first feature noted is the sensation of cold, most pronounced in exposed parts as the extremities, lips, nose and ears. The surface at first becomes pale, due to the contraction of the cutaneous capillaries, the skin is contracted and harsh, "goose flesh" may appear from the stimulation of the pilar muscles and shivering ensues. There is, in consequence, congestion of the internal viscera, which may be sufficiently extensive to cause death. The cerebral congestion may cause the individual to be somewhat exhilirated, and to try to increase his circulation by active movements. As the exposure continues, the sensation of cold is lost, being replaced by a tingling or sense of actual pain, the cutaneous vessels dilate and the surface is covered with a diffuse blush, which gradually deepens, in the distal parts of the circulation, to a purplish, cyanotic hue, which later becomes blanched, although livid blotches of irregular size, shape and location may remain. The hands and feet, nose, lips and ears usually remain livid. If recovery of the victim takes place, chilblains, or intense inflammatory reactions, or even gangrene may develop in these parts. Gradually the tingling and pain are replaced by numbness, which may deepen into actual anesthesia. The pulse, which up to this time may have been normal, becomes soft and weak and irregular in rate and rhythm. The victim may now complain of a sense of oppression in the chest and an irritative cough may develop, associated with a frothy, bloody sputum. Weakness and fatigue now come on, there is no desire for further physical effort, and an intense, overpowering drowsiness comes on, the victim passing into a sleep which deepens into coma and passes into death.

Death usually occurs from gradual cardiac failure, but syncope may be the termination, at times the respiration ceasing before all signs of cardiac activity have disappeared. It is possible that at least a contributory cause of death is the oxygen starvation of the brain and nerve centers, which arises from the fact that the oxygen is less easily dissociated from the hemoglobin at low temperatures than under normal conditions. The actual time occupied in the process of freezing varies, depending on such factors as vigor of constitution, age, bodily protection, and temperature of exposure. Usually several hours are necessary. The combined effect of cold air and dampness is more marked than is that of cold dry air.

Postmortem Appearances. The appearances met with in the body after death from cold are few and are not distinctive except where the exposure has been to intense, freezing temperature. In such cases the surface of the body is extremely pale, but in parts exposed to the air, not merely in dependent parts, livid blotches may be found, which have no regular position, shape, size, or depth, and which must not be confused with postmortem lividities or with the more or less diffuse cherry-red coloration of the skin in carbon monoxide poisoning. The lips, ears, nose and terminal phalanges are usually blue. The skin may be wrinkled, especially about the thicker parts. The pupils are dilated. Rigor mortis appears at various periods after death, largely depending upon the extent of the physical efforts before death, but, as a rule, true rigor mortis appears slowly. Rigidity from freezing may mask that produced by the usual rigor mortis. In the former case, if a joint be forcibly flexed, a distinct crackling sound will be heard, which is not given by joints stiffened by rigor mortis.

On autopsy the blood is found to be of a light arterial hue throughout the body and much more fluid than usual. The heart and the large vessels are unusually full of blood, owing to the driving of the blood from the peripheral circulation. For the same reason the larger viscera, including the brain, but occasionally, excluding the lungs, are deeply congested. Congestion and miliary hemorrhages seem to be found in all parts of the brain, the nerve cells showing marked vacuolization.[1] Patches of hemorrhage have been noted in the gastric and intestinal mucous membranes. When the lungs do show congestion, small hemorrhages and submucous effusions in the bronchial tubes may be found.

DEATH FROM HEAT

While exposure to the direct rays of the sun most frequently causes serious effects of heat, yet exposure to any excessive external heat, if sufficiently prolonged, produces fatal results. Usually the effects of heat exposure are noted during the hot hours of the summer days and when the greatest physical efforts are being exerted, but there are many cases in which the effects are noted during the hours of rest. In cases where the exposure is limited to the heat rays alone, as in the hot, close, stuffy furnace room, factory, bakery, or other highly heated place, the effects are accentuated by a lack of free circulation of the air as well as by a highly humid condition of the surrounding atmosphere.

Symptoms.—There are two forms of severe heat injury, which differ rather strikingly in their clinical manifestations. The first of these is associated with a vascular dilatation and relaxation, while the other is charaterized by a circulatory stimulation and peripheral hyperemia.

1. *Heat Collapse, Heat Exhaustion, or Heat Syncope.*—This type occurs among laborers, soldiers on the march, and especially in persons who are unaccustomed to heavy work but are, nevertheless, attempting to do it. In such cases there may or may not be exposure to the direct rays of the sun. The milder types come on gradually and are associated with a sensation of intense heat, a scanty perspiration, a flushed face, throbbing pain in the temples and a dry mouth. In about ½ hour the subject feels suddenly weak, the surface of the body becomes pale and a profuse perspiration ensues, chilliness is complained of, nausea and vomiting may come on quickly and the patient may have an urgent desire to defecate. In the more severe cases, the symptoms may occur

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[1] Bender, Arch. Neurol. and Psychiat., 1928, **20**, 319.

suddenly or follow those of the milder type. While in the midst of his work, without any warning, the victim may stagger and fall unconscious. The surface of the body is pale, bathed with perspiration, and the skin is cold to the touch; the pulse is rapid, weak and irregular; the temperature subnormal; the pupils are dilated; the respiration may be sighing; and there may be a low muttering delirium. The subject may recover if placed at rest and given stimulating remedies, or the condition may become worse and death may take place from cardiac failure. In a recent article Hall and Wakefield[1] report a study of experimental heat-stroke from which they conclude that "The important acute pathologic change in major heat-stroke, other than that due to the effect of high temperatures per se on the tissues, is a massive increase in lactic acid, with the resulting symptoms of acidosis."

2. *Sunstroke, Heat Apoplexy, Insolation, or Thermic Fever.*—This type of death from heat may be preceded by recognizable symptoms for a few minutes or it may appear very suddenly. The patient complains of headache and a sensation of excessive heat, the perspiration becomes less and less, dizziness is noticed, the face and general surface become congested and the subject suddenly falls unconscious. The surface of the body is red and hot to the touch; the pulse is full and rapid; the respirations may be stertorous or unaltered; the temperature is markedly increased, sometimes reaching 112° to 115° F. The pupils are usually contracted. The patient may lie motionless, or there may be marked restlessness, tremors or convulsions. Death may ensue at once from syncope, or, as is more usual, from asphyxia in the course of ½ hour.

There is a mild type of this form of heat stroke, which has been called *simple continued fever*, *ardent continued fever*, and *hyperthermy*. In such cases the attack usually comes on suddenly, sometimes with a chill, and the temperature quickly rises to 103° or 105° F., or slightly higher. The body is covered with a diffuse blush. Headache, nausea, and vomiting, and either diarrhea or constipation are noted. The pulse is full, respirations are rapid and shallow; and there is much prostration, malaise and pain. Such cases may entirely recover in a few days, but in some of the severer cases, death occurs in three or four days.

Post-mortem Appearances.—In heat exhaustion death is due to syncope, while in sun-stroke it is due to a combination of the effects upon the brain and lungs, or to a mixture of coma and asphyxia. Usually the surface of the body is pale, although there may be patches of lividity in both dependent and non-dependent parts. The autopsy findings will be those due to either syncope or asphyxia, which have been previously discussed.

DEATH FROM STARVATION

Starvation is the result of total or partial deprivation of food, the deprivation being in quality of food as well as in quantity. Such cases may be the result of voluntary action of individuals, may be due to famine, or may be of criminal nature. There are cases in which the taking of food is prevented by some local condition of the jaw, esophagus or stomach, but these are more properly considered under the head of specific diseases rather than of starvation.

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[1] Jour. Amer. Med. Assoc., 1927, **89**, 177.

It is difficult to state the length of time necessary for starvation to produce death, as there are many modifying factors such as age, state of nutrition of subject at the beginning of the deprivation, physical exertion, and temperature of the environment. An arbitrary classification of starvation as acute, when death occurs within 14 days from the withdrawal of food, and as chronic, when death happens after such period, would seem rather unwise. Death has been known to occur after a few days' total deprivation of food, while there would seem to be some authentic evidence that total deprivation of food may be endured, if water be allowed, for some weeks, a month, or even more.

Symptoms.—Although the feeling of hunger may manifest itself a few hours after intake of food and become more and more urgent for 48 hours or more, yet after such deprivation the desire gradually lessens and may soon be completely lost. The patient may remain bright and his intellect clear, or he may become quiet and lethargic, until coma and death result. Emaciation is the most noticeable sign; the eyes are sunken; the face very drawn and thin; the skin is dry; the tongue is thickly furred; the mouth and throat dry; respirations become shallow, weak and frequent; pulse is small, weak and irregular; pupils are dilated and the conjunctivae blood shot. Death finally occurs from cardiac failure.

Post-mortem Appearances.—The skin is thin, wrinkled or shrivelled, and often ulcerated. Bed sores are frequently seen. A peculiar odor is noted about the body. Emaciation is extreme, the muscles being flabby and devoid of fat. On autopsy one notes especially the absence of the ordinary fat deposit beneath the skin, in the omentum and in the usual situations. The stomach and intestines are thin, contracted and empty, while the mucous membrane of the stomach and the upper part of the bowel is diffusely stained with bile. The liver, kidneys, spleen, and pancreas are small and shrunken; the lungs are usually pale and present hypostatic areas of congestion at the base; the heart is diminished in size, the epicardial surface is pale and there is little blood in the heart. The brain substance is usually pale and soft.

CHAPTER VII

DEATH FROM BURNS AND SCALDS: LIGHTNING AND ELECTRICITY

DEATH FROM BURNS AND SCALDS

A *burn* may be defined as a lesion, which results from the exposure of a part (internal or external) or the whole of the body to the action of heat or of chemical substances, the effect of which is more or less marked destruction of the tissues involved. A *scald* is a lesion, which arises from the action on the tissues of a liquid at or near its boiling point, or of the gaseous form of the liquid, such as steam. Burns may be produced by a variety of forms of heat, such as exposure to radiant heat; by the direct application of a flame; by contact with heated solids or solids which have become molten by heat; by friction; by lightning, electricity, and *x*-rays; and by contact with corrosive chemicals, which act by destruction of the tissues. Scalds arise when the source of the heat is in the form of a hot liquid or of a vapor arising from it, the results of the scald differing from those of a burn in that there is no charring of the skin nor any singeing of the hair in the former.

The damage produced, either by a burn or scald, will depend upon the degree of temperature of the heated body, the time of exposure to the action, and, especially, upon the area of surface involved. The following degrees of burns may be recognized: *First degree*, simple hyperemia of the skin, as most commonly noted in cases of sun-burn; *second degree*, characterized by the formation of blebs or blisters, coming on immediately or within a few hours, which may leave a scar without much contraction if the skin only is affected, while marked deformity and disfigurement may result when the lesion heals if the burn is extensive; *third degree*, associated with charring and marked destruction of tissue, which may be followed by gangrene; *fourth degree*, characterized by actual destruction of the parts involved, entire carbonization taking place.

Burns may, therefore, vary in degree from slight hyperemia to charring with almost complete destruction of the part involved. Scalds are usually less severe than burns, although complete destruction of the part or gangrene may follow scalding, as evidenced by the lesions produced by boiling oil, tar, or other tenacious substances with a high melting point. Molten metals are especially destructive, as these adhere closely to the part struck and burn very deeply, multiple foci being often observed owing to the spattering of the molten material. Momentary contact with hot metals may, on the other hand, cause but little damage, owing to the vaporization of the moisture of the skin. The lesion produced by chemical corrosives varies with the type of corrosive employed.

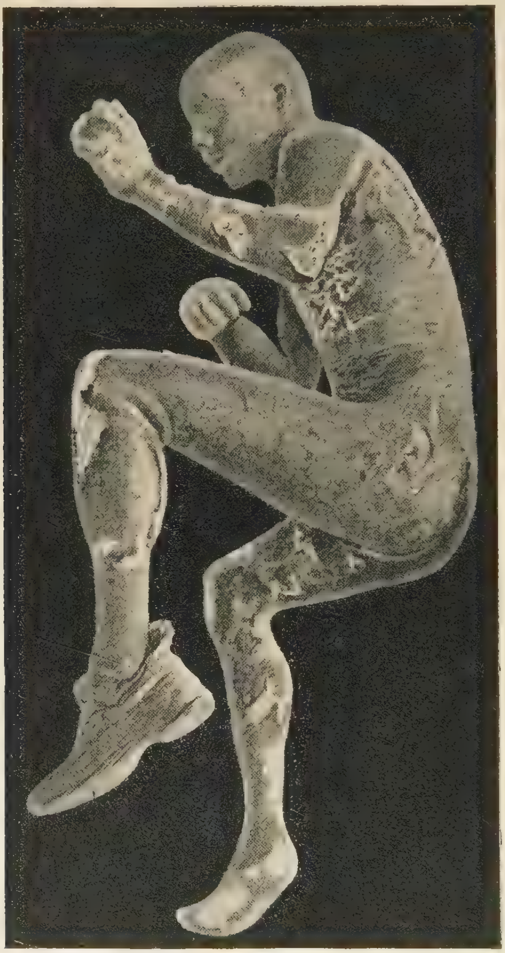

Fig. 9.—Death from burning (Hofmann). Body of a man found, excessively burnt, beside a railroad track. The body had about it an odor of petroleum. No injuries to the body were discovered. Aspirated soot was found in the air-passages, and from this fact it was concluded that the burning had occurred during life. All vestiges of hair had disappeared. The clothing, with the exception of one shoe, had been entirely consumed. The surface of the body was blackened and appeared as though roasted. Here and there the skin was burst.

The burning was evidently the result of applying a match to the clothes, previously saturated with petroleum. Whether the case was one of murder or suicide could not be positively determined. The peculiar position of the body probably developed postmortem, and was due to the contractions of the burnt skin and the musculature drawing up the extended body. Similar abnormal positions have been often observed in cases of deaths from burns.

Thus, with the corrosive acids and alkalies, there may be marked destruction of tissue but there is rarely any vesication; while with such corrosives as phosphorus and metallic sodium or potassium there is usually vesication, followed by destruction of tissues. Sulphuric acid produces a brownish, almost black stain on the skin and the clothing; nitric acid a yellowish color; while hydrochloric acid causes a yellowish or brownish-yellow tint. "The reaction following these chemicals, unlike that from a burn, is soft and moist, the hairs are not burned, nor is there an area of reddened skin which usually surrounds a burn. The spots found upon the clothing usually assist in determining the nature of the chemical used."

External Appearances.—The lesions noted following a burn may present varied appearances. Shortly after a burn is received a red line of demarcation is noticed between the sound and affected tissues. Blisters, more or less widespread over the involved area, are usually present. Even roasted patches of skin or of the deeper tissues may be observed. Singeing of the hair and of the clothing are observed from the action of heat in the form of a flame, and deposits of carbonaceous material render the portion affected black; while radiant heat simply whitens the skin. Burns caused by explosions, especially of gunpowder, may be only superficial but may be accompanied by extensive tattooing due to the driving of unburned powder into the skin. Burns caused by burning oil leave a distinct and characteristic odor and a deposition of carbonaceous material. Persons burned by explosions of fire damp and other gases often have dark carbonaceous particles driven into the skin. The blisters, associated with burns as well as scalds, are characterized by the presence of a fluid containing both albumin and chlorides, a point of distinction from the blisters formed by burns upon a dead body. In the more severe types of burns, there may be, especially near the joints, cracks and fissures of varying depth and extent, such cracks having ragged edges and showing blood vessels stretching across the fissures. Such fissures may open the large cavities of the body and at times their edges may be covered with molten fat. The body of the victim may be contorted, with the legs flexed and the arms in the so-called "pugilistic" attitude.

The appearances produced by scalding will depend upon the degree of heat of the scalding fluid and upon the time of its application. Boiling water and steam produce vesication, but there is no singeing of the hair or blackening of the skin. If the steam be under pressure, there may be no vesication, the skin becoming, rather, of a sodden, ashy color and showing no elasticity. If the fluid be only moderately hot, the lesions may show only an inflammatory reddening of the skin.

With the corrosives, the lesions may, likewise, vary from an inflammatory hyperemia of the skin, occasional vesication, discoloration and staining of the skin and clothing, to ulceration of more or less extent.

General Symptoms.—These are usually called the constitutional effects. As a rule there is more or less collapse and severe shock to the nervous system. The surface of the body is pale, the extremities cold, the pulse rapid and weak, and sensations of chilliness are complained of.

In fatal cases there soon follow dyspnea, gradual cardiac failure, coma, and death.

Causes of Death.—The danger of life appears to depend more, perhaps, upon the extent of surface involved, than upon the intensity of a localized burn. Billroth states that a burn which involves one-third of the surface of the body, regardless of the degree of the burn, is practically always fatal. Death may occur within 24 to 48 hours and is almost always due to primary shock, and is associated with a high temperature, rapid pulse, diarrhea, and all the symptoms of a severe intoxication. If the death occur later than this, it is due, according to Robertson and Boyd[1], to a condition which they call "toxic shock". They believe that there is a toxin produced in burned tissues, in larger quantities in skin burns. This toxin, which they think is of the nature of a proteose, circulates in the blood, either in, or adsorbed by, the red blood corpuscles, and may cause the symptoms seen and, in some cases, death. Should the patient live for a few days, death may be due to infection, tetanus, gangrene, or intestinal lesions, such as duodenal ulcer, which may give rise to a fatal hemorrhage.

In this connection it is to be recalled that children die more quickly than adults, the simplest burns or scalds often proving fatal in the young. The intense pain and shock associated with extensive burns may necessitate the use of opium to control the condition, but should this be used there should be no confusion if coma arises, as it is not an uncommon finding to note a condition of collapse following severe burns. A further condition, noted in cases of extensive superficial burns, is a tendency to an anhydremia, the blood becoming rather markedly concentrated by the pouring out of the body fluid upon the surface of the burned area.[2] Hence, it is rational to assume that a rapid and continued introduction of fluid by all possible channels will cause a gradual return of the blood concentration to normal and a certain improvement in the systemic signs and symptoms.

Post-mortem Appearances.—As far as external signs are concerned, the previous discussion will cover the ground of the appearance of the burned area. "When seen at the morgue the body often presents evidence of immediate death from asphyxia due to smoke and the products of combustion, or from injury due to falling walls. Syncope from fright and collapse from severe injuries doubtless account for many deaths, associated with but few and not striking postmortem findings. If death has not been immediate and has not been due to causes mentioned above, pneumonia, bronchitis, pulmonary edema, or, especially in scalds or in cases where heated air has been inspired, edema of the glottis may be found. Suffocation from carbon monoxide may cause the blood to have an arterial hue totally different from that where there has been simply deprivation of oxygen as in ordinary suffocation. The study of the condition of the blood in those burned to death has not been satisfactory. The results of the different investigators are not in accord. The serous membranes are often hyperemic and may contain considerable effusion. Ecchymoses are at times found in the lungs. Ulceration of the lower end of the esophagus, of the intestines, and especially of the duodenum are common. Death has occurred from hemmorhage from such an ulcer. The heart cavities are generally empty, although the right side may be full of blood. The brain, liver, kidneys, and pelvic organs are often changed, and, as previously stated, focal necrosis may be found in any or all of the parenchymatous organs."[1]

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[1] Jour. Lab. & Clin. Med., 1923, **9**, 1.

[2] Underhill, Carrington, Kapsinow, and Pack, Arch. Int. Med., 1923, **32**, 31.

Medicolegal Considerations.—There are several questions in connection with burns and scalds, which may demand consideration in courts of inquiry. These may be discussed briefly as follows:

1. *Are the Lesions Found the Result of Burning and Scalding?* The characteristic lesions of burning by flame are the singeing of hair and clothing, the deposition of carbonaceous material on the skin and clothing, the formation of vesicles, and the inflammatory area around the vesicle. The extent of the lesions will depend upon factors previously mentioned. Of course, it is to be remembered that friction may be sufficient, in itself, to cause all of the above signs, as sufficient heat may be developed to set fire to the clothing and cause extensive burning of the flesh. So, too, the results of scalding and of burning with corrosives are sufficiently characteristic to permit of definite conclusions. Too much stress must not be laid, however, on the appearance of simple vesiculation, as evidence of direct burning or scalding, as vesication may be produced under certain conditions in which a portion of the body is allowed to remain in contact with a medium in which the heat, consequent upon the fermentation of decomposing animal fluid, is prevented from radiating quickly. Such conditions are, as pointed out by Glaister[2], found (a) where a patient is bed-ridden; (b) where there is neglect in the removal of discharges involuntary passed; and (c) where the vital resistance of the tissues is lowered by disease. However, even in these states, heat is essentially the primary cause of the formation of the vesicles.

2. *Did the Burning Occur Before or After Death?* The answer to this question will depend upon the external and internal evidences and upon the presence or absence of vital reaction in the affected areas. The blister formed by burning or scalding contains a fluid which contains both albumin and chlorides. If the blister fluid does not contain such substances, then it is sufficient evidence that the blister was produced after somatic death had occurred, although as long as there is molecular life in the tissues involved there may be vesication. Post-mortem vesicles contain either air or a non-albuminous fluid. Besides the characteristic contents of the blister, an ante-mortem burn is character-

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[1] Hall and Lewis, "Gunshot Wounds: Burns and Scalds" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, I, 348.

[2] *Medical Jurisprudence and Toxicology*, 4th ed. 1921, p. 234.

ized by the existence of an inflammatory area around the circumference of the vesicle and the floor of the vesicle is swollen and inflamed (reddened). If the body is charred, it will be impossible to tell whether death preceded the burning or not, unless some evidence of other cause of death be found, as for instance a skull fracture associated with a blood clot. If such a finding were observed, one would be justified in assuming that death preceded the burning or, at least, that the victim was unconscious at the time of burning. Careful search for evidence of death from causes other than burning is necessary in many cases, as it is not infrequent to find cases in which a criminal resorts to burning of his victim, after having killed him by some other means.

3. *Was the Burning Accidental, Suicidal, or Homicidal?* The largest proportion of cases of death by burning and scalding are accidental. Injuries due to chemicals are usually accidental. Burns may be intentionally inflicted or an attempt may be made to cover up a crime by the destruction of the body by fire; while chemical agents, which cause burns, may be used homicidally to cause death, or to disfigure, or may be taken suicidally. Suicide by burning is, however, known. In such cases the victim may saturate the clothing with oil and apply a flame or may rush intentionally into a burning building.

In arriving at an answer to this question, all the circumstances surrounding the case must be investigated. The position of the body, the condition of the clothing, evidences of a struggle, depth and character of wounds on the body, and postmortem evidences must be studied. The time necessary to consume a body by fire depends upon many factors, so that a definite answer is difficult, but it may be safely stated as from 10 to 12 hours under ordinary conditions.[1] A complete analysis of the ashes of the burned material may result in the detection of a crime, or, at least, of evidence of the destruction of an animal body, the presence of a large amount of calcium phosphate in the ashes being very significant.

DEATH FROM LIGHTNING AND ELECTRICITY

From the earliest times the deadly effects of lightning have been matters of more or less common knowledge. The bodies of those struck by lightning were either left to decompose or were buried on the spot where they were killed. Mythology offers many illustrations of the belief that those killed by lightning had incurred the wrath of Jupiter. So, also, many of our savage tribes used various incantations to protect themselves from the thunder and the lightning.

Deaths by lightning occur mainly in the spring and summer when thunder storms are common. The United States Mortality Statistics of the Registration Areas show that the average deaths by lightning in the years 1901 to 1905 were 98 or 0.3 per 100,000 of the population; in the period from 1906 to 1910 there were 154; in 1913, 317; in 1914, 287; in 1915, 231; and in 1916, 340. In France from 1854 to 1864, there were 967 deaths from lightning; while in Prussia there were 819 deaths reported between 1869 and 1878. For the decade 1901–1910 the Registrar General of England and Wales reported 124 deaths from lightning, a yearly average of 12.4 deaths or 0.36 per million of the population.

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[1] See Haines, "Destruction and Attempted Destruction of the Human Body by Fire and Chemicals", *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, 2, 876.

As regards the deaths from electricity, it might be expected that the number of deaths from this cause would gradually increase as the use of this agent becomes more prevalent. There is, undoubtedly, a better knowledge of its effects and more general care taken by those coming in contact with it, yet there has been a steady increase in the number of deaths from electricity during recent years. According to Naville and de Morsier[1] about 300 electric accidents occur annually, while Boruttau[2] states that 220 were injured by high-tension currents in Germany from 1906 to 1915; and in England the reports for 1901 to 1910 show 183 deaths[3]. Jex-Blake[4] states that 200 are annually killed by electricity in all Europe. In the United States fatalities from electricity are far greater as shown by the report of the Engineering Committee of the Conference on Electric Shock[5]. In 1915 there were 515 deaths; in 1916 586; in 1917, 654; in 1918, 754; in 1919, 748; in 1920, 822; in 1921,741; in 1922, 842; in 1923, 954; and in 1924, 975. These figures indicate more or less of a steady increase in the number of deaths, but the death rate per 100,000 stays about 0.9.

Since the days of Franklin and his kite the relationship between frictional electricity and lightning has been well established. While it is true that the effects of lightning and electricity on the body differ in many respects, largely on account of the variation in the method of injury and the difference in intensity of the electric charge in the two cases, yet there is some resemblance between these effects and the causation of death from these sources.

Exposure to Lightning.—Like other forms of electricity, lightning follows the path of least resistance and will naturally seek out good conductors if they be in the neighborhood. While this statement is undoubtedly true, yet it must be remembered that lightning may not always select the most attractive conductor but may show vagaries, as the following statements of Tourdes[6] as cited by Woodman and Tidy[7] indicate: "In 1869 three soldiers sat under a tree during a storm. They were struck down by lightning, and two were killed on the spot. There were loftier trees in the neighborhood; a lightning conductor was not far off, and an iron railway bridge and a river were near. The electric fluid struck the lower tree, and passed through the bodies of the men, in place of being carried off by the surrounding conductors."

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[1] Ann. de mèd. lèg., 1927, **7**, 245.

[2] Vrtljschr. f. ger. Med., 1918, **54**, 1.

[3] See "Death and Injuries by Lightning and Electricity" by Jelliffe in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **I**, 261.

[4] Brit. Med. Jour., 1913, **1**, 425.

[5] Jour. Indus. Hyg., 1928, **10**, 110.

[6] Ann. d'Hyg. Pub., 1871, **1**, 478.

[7] *Forensic Medicine and Toxicology*, 1877, p. 868.

For the above reason it is usually found that those struck by lightning are near some conductor, usually a tree, a tower, a steel bridge, mast of a ship, or other object. Metallic material is especially attractive for lightning, so that it was quite common some years ago to find every house, barn, church, etc., equipped with so-called "lightning rods" to conduct the lightning to the ground and thus lessen the danger to the building itself. Such simple objects as metal plates, metal ferrules or sticks of umbrellas and metal tops of tent poles have proven dangerous in thunder storms. While more accidents naturally occur to those out of doors during a storm, yet it is not infrequent for persons indoors, especially those near a door or window to be struck, their danger increasing, of course, with the nearness of some metal conductor. Further, it has been found that the ideas expressed by Arago that, when lightning struck men or animals who were located either in a straight line or in an open curve, the most severe effects of the stroke would be manifest at the ends of the line.

Symptoms of Lightning Stroke.—When struck by lightning the individual may be simply stunned, may be rendered unconscious at once, or may be killed outright. If not killed the following signs may be noted: The face is usually flushed and reddened; there are blinding sensations in the eyes; buzzing in the ears; tremors, which change to severe convulsions in which the face becomes cyanotic and the pupils dilated; the respiration is usually stertorous and may be rather slow; the pulse is feeble and may be rapid or irregular.

The main effects of the stroke are shown upon the nervous system. These may consist of simple mental shock or intense and prolonged nervousness. Jelliffe describes this picture as follows: "If an electric bolt strikes in the near vicinity, a mild stunning may be experienced, with a sense of suffocation, which will in all probability pass off quickly, or in some sensitive and neurotic persons an attack of nervous crying may be brought on. In such patients suppression of menstruation has been produced, and cases of abortion have been reported. In the severer cases loss of consciousness, which may be transitory or much prolonged, is not rare, and this is frequently followed by various phenomena, ranging from numbness and prickling of various areas of the body (paresthesiae) to anesthesia or analgesia of the extremities or side of the face, with difficulty of mastication. Paralyses are by no means uncommon, occurring in the muscles of the arms and legs; ptosis and strabismus have been reported; deafness and loss of smell and taste, with paralysis of the bladder and rectum, and motor inco-ordination may be present. Polyneuritis has resulted." Psychoses, usually of the maniacal type, have been reported as occurring after lightning stroke. In most cases there is a dread, amounting oftentimes to a delirium of terror, which is experienced during every thunder storm.

External Lesions.—A great variety of external lesions from lightning stroke have been reported in the literature. In some cases death has been so sudden that there may be no external evidence of the stroke. Wounds of almost any type may be noted, especially characteristic being the disruptive lacerations found at the point of entrance and exit of the bolt. The hands and feet are often the seat of such lesions, but other parts of the body are similarly affected. Some of these wounds may appear as lacerated punctures closely resembling stab wounds made with a blunt instrument, so that confusion as to the cause of the wound may easily arise. Often there are observed minute, bluish, punctiform spots on the hands and feet or there may be numerous ecchymoses in various locations. While fractures of the bones are not commonly found, yet there are cases in which there may be single or multiple fractures of all types. Burns are not infrequently found on the body, and these may vary from simple vesication to charring of the flesh. While many of these are produced by the burning of the clothes, yet others are caused by the action of the lightning itself. Taylor[1] cites a case of Geoghegan

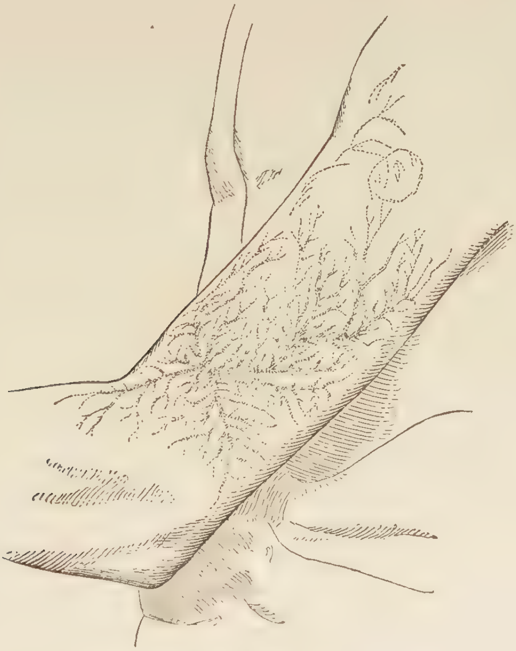

Fig. 10.—Arborescent-like markings on arm from lightning stroke. (From J. Dixon Mann, "Forensic Medicine and Toxicology," Charles Griffin & Co., Ltd., London, Publishers.)

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[1] *A Manual of Medical Jurisprudence*, 12th Amer. Edition, 1879, p. 490. See, also, Langerhans, Virchow's Archiv, 1862, **24**, 200.

which indicates "that the dress may be burnt without the surface of the body being simultaneously injured; and further, that a burn may be produced on the body, although the clothes covering the part have escaped combustion." These burns may assume almost any shape, some being linear, others patches, while still others may be in the form of reddish streaks or even arborescent-like areas. These radiating reddish streaks are supposed to be especially characteristic of burns from lightning. These burns, especially those about the scalp and face, may be associated with singeing or burning off of the hair. In the passage of the lightning through the body, the point of entrance is usually markedly burned, while the above-mentioned streaks and lines of redness or even of ecchymosis may represent the course of the bolt. In passing out of the body, the lightning may tear the clothes or shoes from the body or there may be little or no injury to these coverings. Should there be metallic objects in the pockets or about the person, impressions of such may be noted on the skin or these articles may be found fused. Occasionally these metal objects assume marked magnetic properties.

Internal Lesions.—Unfortunately the literature on the post-mortem appearances following lightning stroke is very meager. Death is usually due to shock or syncope, although the injuries or burns received may be sufficient to bring about the fatal result. Hence, the findings may be almost negative or may be directly related to the severity of the injuries received. The brain and its membranes may be anemic or congested, and in cases where direct injury to the brain has occurred as a result of fracture or burning, much destruction of brain tissue may be found and effusions of blood may be noted beneath the dura or in the brain itself. Blood vessels may be ruptured in various parts of the body and various viscera may show marked congestion or may even be ruptured. Practically no studies of the microscopic findings have been reported, although Schmitz states that parenchymatous inflammation of the internal organs may occur. As to the question of rigor mortis following lightning stroke it is to be said that the statement of Hunter, that there is an absence of rigor mortis, must be contradicted. In a case observed by Rindfleisch[1] rigor mortis appeared in 12 hours after the stroke, while Dunscombe-Honiball[2] reports rigor mortis in from 8 to 20 hours in his cases. It is possible that some may have reported rigor mortis as being absent, owing to the fact that it may have been present and disappeared at the time of examination. This point is covered by Mann[3] when he says: "Cadaveric rigidity not unfrequently occurs at the usual period; sometimes it comes on immediately after death, and in this case is evanescent." While the blood in some cases does not coagulate promptly and has been described as dark and fluid, yet it may coagulate as usual after death, most cases showing some clotting at least.

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[1] Virchow's Archiv, 1862, **25**, 417.

[2] Brit. Med. Jour., 1900, **1**, 1153.

[3] *Forensic Medicine and Toxicology*, 1893, p. 240.

DEATH FROM ELECTRICITY

At the outset it is to be said that the effects of an electric current will depend upon the relationship between the voltage (tension or pressure of the current), amperage (quantity of the current) and the resistance offered by the conductor to the passage of the current. This relationship is stated in Ohm's well-known law which asserts that when a continuous current is flowing through a given conductor, the temperature of which is kept constant, the ratio of the electro-motive force (in difference of potential) existing between the terminals of the conductor and the current carried by the conductor is a constant, no matter what the value of the current may be. This constant, the value of which depends only upon the nature of the conductor, is denoted by the letter R and is called the electrical resistance of the conductor, the unit of which is the ohm. If we indicate by the letter E the electro-motive force or volts and by the letter C the quantity of current or amperes, we may write this law in the form of an equation as follows: $\frac{E}{C} = R$ or $\frac{\text{Volts}}{\text{Amperes}} = \text{Ohms}$. For convenience this equation is sometimes written $\frac{E}{R} = C$. We shall see that there are other factors, such as the type of current (alternating or direct), length of contact with the current, and the direction of flow of current, which must be considered in our discussion of this subject.

It is clear that one of the most important protective influences against the passage of electric currents through the body is its high resistance. The exact figure for this resistance is somewhat uncertain as there are many circumstances which may modify it. Thus, Jelliffe states "Thus, when the epidermis is perfectly dry, its resistance to the passage of electric currents has been shown by Jolly to be very high, measuring, in Siemen's units, from 8000 to 40,000 ohms (Herold). Dry skins are more resistant, also hard and oily skins. Moist, soft and perspiring skins have much reduced resistance. If the skin is thoroughly moistened, the resistance of the body may register but 500 ohms, and skins treated with alkalis that remove the fat are less resistant." These figures are at variance with those given by Glaister, who says: "The hands, when perfectly dry, offer a resistance of 30,000 ohms; when perspiring ordinarily, of about 10,000 ohms; and when dripping wet, of only 7000 ohms." The degree of this resistance may be indicated by such comparisons as the following: One of the Atlantic cables offers a resistance of about 8000 ohms; while Beard and Rockwell report the computation that an inch of the sciatic nerve has eight times the resistance of the Atlantic cable.

While the voltage of an electric current undoubtedly bears an important relation to the type of accident or injury or even of death, yet this factor is modified to a great extent by the character and the amperage of the current. While there is no question about the danger of the high tension current, there has been some doubt as to the harmfulness of the low tension currents. That the latter currents do cause fatal accidents is shown by the reports in the literature. Thus, as stated by Jaffé[1], "Jellinek says that currents of more than 25 volts should be considered dangerous. He observed a fatal accident in Vienna caused by a current at 60 volts. In the case reported by Capello and Pelligrini the tension was even lower, 46 volts. Jex-Blake speaks of 65 volts as being dangerous when the current passes through the heart. Of the 300 electric accidents which occur annually in France, 100 are caused by currents at low tensions. In Switzerland, accidents caused by low voltages seem to be more common than those caused by high tensions. Kawamura, who studied 110 electric accidents in the Mitsui mines of Japan, found that sixty-nine persons were injured by currents of low tensions and forty-one by currents of high tension. Schridde saw thirty-seven fatal accidents caused by alternating currents of from 220 to 250 volts." From experimental evidence it appears that the essential features of danger from electric currents are the amount of the current and the duration of its contact. As Jelliffe says, "High voltage, long duration, and close contact usually cause severe systemic shock, burns, coma, or death. Moderate intensity with medium duration and imperfect contact produce burns of the second degree or less, momentary unconsciousness, slighter grades of shock, with paresthesia. If the currents are of low intensity, the duration and closeness of the contact less, only first degree burns are produced, there is rarely disturbance of consciousness and the tingling paresthesiae are milder or even quite fugitive. Very short periods of imperfect contact with low intensities are apt to cause paresthesiae only." The experiments of Peterson seem to indicate" that if a continuous current, say of 1600 volts electromotive force, is sufficient to cause death, then an alternating current of much less than half that voltage must be fatal under the same conditions." In his experiments dogs were not injured by continuous currents of 1400 volts, but alternating currents of 300 volts caused great distress in 2 seconds. With 4000 vibrations a minute, and in the strength of 570 volts, the dogs were killed at the expiration of 3 seconds. With the same voltage and an increasing number of interruptions the fatal quality is manifest. These same points were shown in the physiologic experiments made preparatory to the introduction of the electrocution laws in New York in 1889. "It seemed fairly well established that no human being could withstand the alternating current of 1500 volts, and 300 had produced death, while for the continuous current it was necessary that over 3000 volts were requisite to bring about fatal results." In the actual practice of electrocution, 1700 volts, alternating current, is the usual amount employed.

External Lesions. As the voltage of the current with which workmen and others may be brought in contact vary so greatly according to the use to which the current may be put, the lesions found will also vary as indicated in the preceding paragraph from very slight paresthesiae, through stronger nervous phenomena with first or second degree burns, to very severe burns, with shock, coma and death. It is to be remembered that there may be associated injuries, such as fractures, dislocations, wounds of various sorts, and other lesions, produced which are indirectly caused by the electric shock, as the subject may fall from a distance owing to loss of muscular control on coming in contact with a "live wire". These injuries are not to be regarded as direct results of the action of the electric current. The direct action of the current may cause very violent muscular contractions, subjects often being thrown several feet and sustaining almost any variety of surgical injury; or the muscles in contact with the electric conductor become tetanized and continue to remain in contact with the current and thus complete charring or burning off of a hand may result; or, in very mild cases these muscular contractions may be evident only in the form of tremors.

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[1] "Electropathology", Arch. Path. 1928, **5**, 837. This article contains a very complete bibliography of the subject.

Internal Lesions.—There would seem to be practically no signs that may be regarded as pathognomonic of death from electricity. Kratter[1] from his experiments on mice, guinea-pigs, rabbits and other animals, concluded that, when taken in conjunction with the external burns, the following signs were really pathognomonic: Subpericardial and subpleural ecchymoses, and more particularly subendocardial ecchymotic extravasations, combined with bloody emphysema of the larger bronchi. In his animals, rigor mortis appeared very rapidly and persisted for a distinct period of time; no changes in the morphology of the blood were observed except at the points of contact of the electrodes. Corrado in his work with dogs has found certain changes in the external shape and configuration of the body of the cells of the brain and spinal cord, and, also, changes in the cytoplasm and of the dendrites. However, as these changes are as yet unconfirmed by the reported examinations on man, we shall not discuss them. Werner[2] described the brain at autopsy as being very hot, and reports a temperature in the brain of 145° F.

In his experimental work on animals MacMahon[3] found that "the only positive and constant gross finding in the animals that were given a single fatal shock was marked congestion of the lungs, liver, kidneys, spleen and heart. Hemorrhages were frequently seen in the psoas, iliacus and gluteal muscles, and were usually bilateral. The meninges were injected, and two of the animals had petechial hemorrhages in meninges of both brain and cord." MacMahon, in discussing the pathologic histology, says "There is congestion of the heart, spleen, kidneys, and adrenals, congestion at the periphery of the lobules of the liver and congestion and petechial hemorrhages in the lungs. No constant lesion is present in the heart. The histologic study of the central nervous system of the animals which received a single fatal shock reveals no constant changes other than capillary injection and occasional petechial hemorrhages. In the guinea pig we find definite lesions that vary somewhat in the different animals, depending largely on the severity of the shocks, the number of shocks and the duration of time that elapsed before death. The lesions are best studied in the cord and peripheral nerves including the medullated nerves to the diaphragm and heart, but are also seen within the medulla, in the tracts leading from the pons to the cerebellum and also in the lower portion of the internal capsule. It is the white matter of the cord that is most seriously affected, and in the majority of animals the lesion is greatest in the posterior columns. The earliest change consists in a swelling of both the axis cylinders and myelin. The picture within the cord differs considerably depending on whether it is viewed from a cross-section or a longitudinal section. In the former the gray matter may show little or no change, whereas the surrounding fiber tracts which comprise the white matter may be riddled with different sized vacuoles. In the longitudinal section the cord has the most bizarre appearance. Axones may be followed only for a short distance; they are irregularly swollen and tortuous and appear to taper off at the ends as though disrupted. In the more advanced lesion where the process has progressed farther, there are foci of marked myelin degeneration heavily infiltrated with phagocytic endothelial leucocytes, scattered polymorphonuclear leucocytes and a few extravasated red blood cells. The nerves show similar though less marked lesions."

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[1] *Der Tod durch Elektricitat,* Vienna, 1896, p. 61.

[2] New York Med. Jour., 1923, **118**, 498.

[3] Amer. Jour. of Path., 1929, **5**, 333. See also, Schneider, Wien. Med. Wchnschr., 1929, **79**, 53.

From the reports of autopsies on some of those electrocuted, certain changes are noted in the brain and its membranes. Thus, in Shrady's record of the findings in the case of Kemmler, the first officially electrocuted criminal in New York State, we find the following: "Capillary hemorrhages were noted on the floor of the fourth ventricle, the third ventricle, and the anterior part of the lateral ventricles. The circumvascular spaces appeared to be distended with serum and blood. The brain cortex beneath the area of contact was notably hardened. The vessels of the corpora striata were notably enlarged at different parts of their ramifications. The pons was slightly softened. The spinal cord showed no gross lesions." The examinations of Van Gieson on the bodies of Jugigo, Smiler, Wood and Slocum showed nothing especially abnormal in any of the viscera that could be related to the cause of death. His report on the brain of Jugigo is as follows: "The pia was uniformly thin and moderately congested. The blood was fluid throughout. The vessels at the base of the brain were normal. The gray matter was normal. Floor of the fourth ventricle at upper half contained some dilated vessels, and on the left side there were a number of minute radiating petechial spots from 1 to 2 mm. in diameter. These small petechial extravasations show small masses of extravasated red blood-cells situated for the most part in the perivascular spaces just beneath the ependyma." His conclusions are "(1) The passage of an electric current of the pressure employed in these cases (of approximately from 1400 to 1700 volts) and in this manner does not do any damage to any of the internal organs, tissues, or muscles. None of these parts are lacerated or changed in volume; neither are there any gross chemical or morphologic changes or alteration of their finer structural features. (2) The local thermic effects of the electrodes are limited to the scarf skin. (3) The occurrence and distribution of the minute hemorrhagic spots are not uniform or constant features in these cases; and as they are found after death from a great variety of causes, they cannot properly be regarded as positively characteristic of death by this method."

Causes of Death by Electricity.—Although many different theories have been advanced as to the causation of death from electricity, it is highly probable that the chief lethal effect of both the continuous and alternating currents is due to their action on the heart, although it must be stated that death may take place in different ways according to the path travelled by the electric current. The conclusions of Cunningham[1] state the case very clearly as follows: "(1) Industrial electric currents which traverse the whole body transversely or longitudinally in sufficient intensity kill because fibrillary contraction of the heart is produced, and not, as has been hitherto surmised, by producing a total paralysis of that organ or by killing it outright. (2) Such currents neither kill the central nervous system outright nor paralyze it instantaneously. Death of the nervous system from such currents is due to the total anemia following a sudden arrest of the circulation. (3) In rare cases, when an electric current traverses only the cerebro-cervical portion of the nervous system, in considerable intensity and for a considerable length of time, it may kill by asphyxia, consequent on a more or less complete inhibition of the

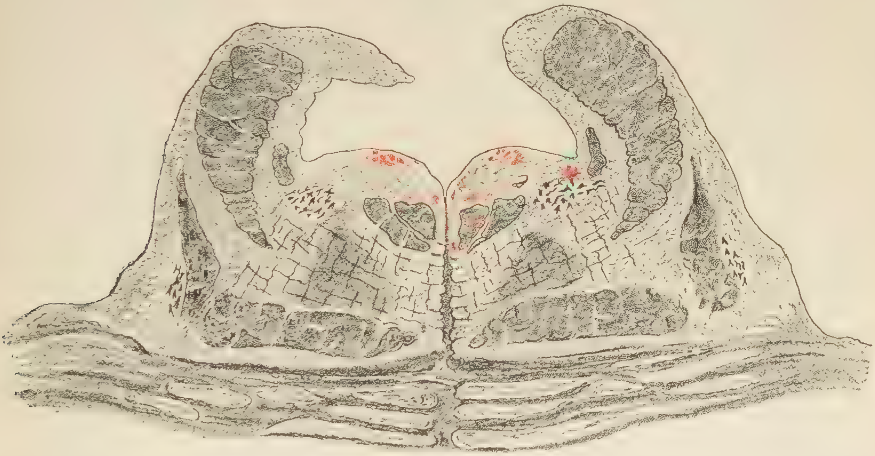

Fig. 11.—Showing the character and distribution of the petechial spots in the floor of the fourth ventricle in the case of Schichiok Juggio. (Van Gieson.)

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[1] New York Med. Jour., 1899, 70, 581 and 615.

respiratory movements, which occurs chiefly during the passage of the current. No existing facts warrant the conclusion that the medullary respiratory center is paralyzed or killed in such conditions. (4) Strong electric currents applied to the surface of the skin affect the heart in the same manner as currents of less strength do when they are applied directly to the exposed heart. (5) It may be possible for an electric current of enormous intensity and electromotive force to produce instantaneous heat coagulation of the cellular constituents of the body. Industrial currents do not kill instantly, although, as a result of their action, death rapidly occurs." Naville and de Morsier[1] emphasize the importance and frequency of syncope as a cause of death from electricity.

A caution should be inserted here in regard to handling those dead from the action of industrial currents. Some insulating material, such as rubber gloves, blankets, or cloths, should be used in handling the wire and in moving the body. The subject must not be touched with the naked hands, but may be moved by the clothing or wrapped in blankets, or removed from contact with the earth by placing a board under him. "Live wires" should be removed by means of a stick or by handling with rubber gloves. Failure to observe these precautions has, more than once, resulted in the death of those going to the rescue.[2]

Treatment.—As soon as the victim is removed from contact with the source of electricity, he should be laid on his belly, the tongue pulled forward, and any foreign bodies in the mouth removed. Artificial respiration by the Schäfer method should then be instituted and continued for at least three hours if necessary, before giving up the attempt at resuscitation.[3] After the patient has been revived, the after treatment is symptomatic and supporting. The burns, if present, are treated in the usual manner.

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[1] Ann. de mèd. lèg., 1927, **7,** 245.

[2] For a discussion of various points connected with the question of death from lightning and electricity see Jellinek, *Elektropathologie,* 1900 and the Goulstonian Lectures by Jex-Blake, Brit. Med. Jour., 1913, **1,** 425, 492, 548 and 601.

[3] For details of this method see Treatment of Carbon Monoxide Poisoning. See also, Maclachlan, Jour. Amer. Med. Assoc., 1924, **83,** 756; and Drinker, Ibid., 764.

CHAPTER VIII

WOUNDS AND INJURIES IN THEIR MEDICOLEGAL ASPECTS

In surgery a *wound* may be defined as a solution of continuity of the true skin, the mucous membranes, or the surfaces of the internal organs. This is a much narrower meaning than is embraced in the medicolegal conception, which comprehends all lesions of the body. "Any lesion of the body, whether cut, bruise, contusion, fracture, dislocation, or burn," is regarded by most jurisdictions as a wound. In some of the earlier English cases, the legal definition of a wound was more restricted than is the case today. Thus, in Moriarty *v.* Brooks[1], Lord Lyndhurst said: "The definition of a wound, in criminal cases, is an injury to the person, by which the skin is broken. If the skin is broken, and there was a bleeding, that is a wound." It will be seen that very severe injury might be inflicted upon a person and, yet, such a case would not fall under the statutes concerning wounding, if this definition were to control. Later the interpretation was extended to cover internal lesions, such as fractures. Thus, in the case of Rex *v.* Smith[2], where the left jaw was fractured in two places by a blow with an iron hammer, and the skin inside of the mouth was broken, Judge Park said: "There must be a wounding; but if there be a wound, (that is, if the skin be broken, whether there be an effusion of blood or not), it is within the statute, whether the wound is external or internal." Under the same ruling dislocations and lesions of the internal organs would now be regarded as wounds. It is clear, therefore, that the true legal interpretation is that a wound must be an injury which does damage to the part affected. The statutes often cover the possibilities of misinterpretation by stating: "Whosoever shall, by any means whatsoever, wound or cause grievous bodily harm to a person, etc." That the old idea, as handed down by Lord Lyndhurst cited above, may prevail in some of our courts, is shown in a recent Virginia case[3] in which an appeal was taken to the Supreme Court following a conviction for feloniously wounding another. It was contended by the appellant that the injury received, which was shown to be a bruise without breaking the skin, did not constitute a wounding within the meaning of the act. Although the statute contained the words, "or by any means cause him bodily injury," the Supreme Court reversed the decision of the lower court, stating that "The trial court in the present case erroneously refused to instruct the jury that unless they believed beyond a reasonable doubt that the injury suffered by Collins from the blow caused the absolute parting and breaking of the skin, they could not find the accused guilty." Probably as acceptable a definition of a wound from the medicolegal point of view, as now understood, is that of Taylor,[1] which runs as follows: "In a medicolegal sense, a wound implies a breach of continuity in the structures of the body, whether external or internal, suddenly occasioned by mechanical violence."

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[1] 6 Carrington and Payne's Reports, p. 684.

[2] 8 Carrington and Payne's Reports, p. 173.

[3] Harris *v.* Commonwealth (Va.), 142 S. E. 354.

NATURE OF WOUNDS

From their nature or relative gravity wounds may be either *slight*, *dangerous*, or *mortal*. The results of a slight wound may at first seem very trivial but may become dangerous or even fatal owing to intercurrent infections or a feeble general condition of the victim. However, what the court wishes to know is what is the nature of the wound at the time of its infliction and what are the chances of death being more or less immediate.

By a *slight wound* is meant one in which the lesion is neither extensive nor serious, one in which there are no parts injured which are important to the usual functions of life, and one which heals quickly and leaves no lesion or deformity behind. By a *dangerous* or *severe wound* we imply one which is rather extensive or serious with reference to the part involved, one which is not exempt from danger and requires more or less surgical interference in its cure. Such wounds do not put life in imminent danger and have been styled as "wounds causing grievous bodily harm." By a *mortal wound* we understand one whose consequence is either immediate death or death within a short time after infliction from shock, hemorrhage, or injury to a vital part. It is to be remembered, however, that a slight wound may become dangerous or even mortal from secondary infection, that a dangerous wound may become mortal from some complication, so that a statement relative to the nature of any specific wound must have reference to the wound at the time of its infliction.

In cases of criminally inflicted wounds, one of the first points which the authorities are anxious to have cleared up is whether or not the wound is mortal. Upon the answer to this question will depend to a large extent the disposition of the one suspected of the crime, that is whether or not he shall be confined in prison or liberated on bail pending the investigation. In his study of the wound and the parts involved and in forming his conclusions as to the nature of the wound, the physician should not be too quick to give his opinion, because many circumstances may be present which will alter the possibilities in the particular case in hand. With many wounds there is no difficulty in stating that they are mortal, but with others the prognosis will depend to a large extent upon the rapidity and skillfulness of surgical intervention. Hence, a dangerous wound may become mortal or may be corrected so that death does not intervene. The mere fact that the physician may have had or seen cases, which appear to all intents and purposes to be exactly similar to the one in hand, and which have ended fatally or have recovered, may lead him to make a definite statement which may later be regretted. The point involved is that one cannot predict the possibility of recovery from dangerous wounds by reference to similar cases; every case must be decided from the conditions actually present. As Bohn[1] remarks: It has never been demonstrated, and indeed in the nature of things it never can be proved, that a wound from which there is a recovery, is precisely similar to one which has proved fatal, although externally they may be similar in every respect.

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[1] *A Manual of Medical Jurisprudence*, 12th Amer. Ed., 1897, p. 247.

There are certain conditions which may cause a change in the nature of the wound as inflicted, or in other words may cause a questionably mortal one to become an inevitably mortal one, may transform a dangerous wound into a mortal one, or render a slight one dangerous. Among these conditions may be mentioned the following, as discussed *in extenso* by Beck: (1) The constitution and age of the patient, and his antecedent or co-existent maladies may exercise a harmful influence on the injury received; (2) the excitement of the patient and his negligence or delay, as indicated by his refusal to undergo proper treatment, by his errors in diet or proper care, by not following the instructions of the physician, by tearing off bandages or dressings, etc., may render slight wounds dangerous and dangerous ones mortal; (3) exposure to excessive cold or heat, to rain or snow storms, and to an unhealthy climate may alter the nature of the wounds and increase the possibility of death. Such cases are especially noted in military campaigns.; (4) the ignorance or negligence of the surgeon in charge may aggravate or change the condition of a wounded patient.

CHARACTER OR TYPE OF WOUNDS

"Wounds should be carefully studied, for the evidence given by them is important. The character of the wound; the probable method of infliction, the weapon employed, the direction in which the vulnerating force was applied; whether the wound was self-inflicted or caused by another, whether it occurred during life or after death must all be considered. The evidence wounds give may be of greatest importance. Usually wounds tell their story in no uncertain tongue. Too much care cannot be employed in determining every characteristic of a wound. Its position and relation to definite fixed points of the body, the character of its edges, the color of the adjacent tissues, its size in all directions should be carefully determined in order that a thorough and absolute knowledge may be had from which deductions can be drawn as to the character of the vulnerating force and the way and direction in which it was applied."[2]

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[1] Quoted by Beck and Beck, *Elements of Medical Jurisprudence*, 10th ed. 1851, 290.

[2] See Balch and Lewis, "Wounds" in *Legal Medicine and Toxicology*, by Peterson, Haines & Webster, 1923, I, 283.

Wounds may be either *open*, those in which there is a solution of continuity of the skin, or *subcutaneous*, in which the skin is unbroken although the underlying tissues may be injured. Open wounds, depending largely upon the type of weapon which produces them, may be classified as follows: (1) Incised; (2) punctured; (3) lacerated; (4) contused; and (5) gunshot.

Although it is not necessary to prove that a weapon has been used in producing a given wound, yet considerable importance is attached to the possibility of the use of a weapon, as this implies intent to injure and, therefore, malice. In this connection it should be stated that medical witnesses should be guarded in their statements as to the causation of a wound by a particular weapon; all that is justified is the opinion that it might have been caused by it or by one similar to it.

1. Incised Wounds.—An incised wound, in common language a cut, is defined in surgery as "a solution of continuity without loss of substance." Such wounds are produced with cutting instruments, such as knives, scissors, hatchets, scythes, swords, etc., or with objects having more or less sharp edges, such as pieces of glass, earthen ware, metal, or even a sharp piece of wood. While the sharp instruments produce clean cut wounds with smooth edges, when the weapon is dull or somewhat blunt the wound may have a more or less serrated edge. Heavy weapons, such as hatchets and axes, may cause much contusion and laceration, although the wound is essentially an incised one.

While the character of the weapon may be suggested by the appearance of the wound, yet the form of the wound will depend, also, upon the manner in which the particular weapon is used. If the weapon is driven into the tissues as in stabbing with a single or double-edged instrument (in which case we have a combination of an incised and a punctured wound), the action is really that of a wedge, the size of the wound being less than the size of the weapon and the form being more or less fusiform, owing to the fact that the retraction of the tissues is greater in the middle than at the ends; while if the instrument is used in cutting, the form will be more linear, although there will be some "gaping." Incised wounds, made by falling on sharp pieces of glass or crockery, may show a margin more or less contused and an irregular edge rather than a direct linear incision, owing to the fact that the wound is caused more by the pressure of the object than by a cutting movement. However, in such cases it may be a difficult matter to differentiate the wound as one caused by a sharp object rather than by a dull, irregular edged knife. In parts of the body where the skin is tightly stretched over the bone beneath, as the forehead, the zygomata, or the jaw, a sudden impact of a golf ball or a fist may cause a wound which is difficult to distinguish from a true incised one.

The edges of the true incised wound are usually straight and regular, although they may be curved or even zig-zag, are usually everted and the sides of the wound are retracted. Such wounds have a tendency to bulge in the center, as the gaping is due to the elasticity of the skin and the contraction of the muscles and is greater in the center of the wound. However, the amount of the gaping will depend upon the course of the cut; if this run parallel with the fibers of the muscles there will be less than when the wound runs directly or obliquely across the muscles. It is to be recalled that in some cases, especially in wounds of the scrotum, the skin is inverted instead of everted, owing to the contraction of the muscle fibers immediately beneath.[1] In incised wounds there will be evidence of more or less bleeding of an arterial type and the blood will be found on various objects about the person or in the room, depending upon the amount of spurting from the arteries cut. Coagula and clots of blood will be found in the wound. The muscular and cellular tissues about the wound are usually deeply colored by the effused blood. The severity of incised wounds depends upon the extent of the hemorrhage associated with them. Of course if the wound is not seen until some time after its infliction, evidences of repair may be present and some of the above characteristics may have disappeared. However, in the cases of medicolegal importance death or very serious injury has occurred, so that the examinations are quickly made.

2. Punctured Wounds.—A punctured wound is made by an instrument which penetrates the skin and enters the body to a more or less extent. Such wounds are characterized by narrowness as compared to depth and, consequently, may be made by any weapon which leaves a narrow and deep wound. Tourdes has classified punctured wounds into 4 classes, according to the type of weapon used, as follows: (A) Wounds made by cylindric or conical instruments; (B) wounds made by sharp pointed and cutting instruments; (C) wounds made by instruments with ridges and edges; and (D) wounds made by irregular perforating instruments.

(*a*) *Wounds Made by Cylindric or Conical Instruments.* If the instrument be a fine needle, it merely penetrates the tissues and does not divide them, although it does separate the anatomical elements. In such cases there may be no mark of a bloody path and the wound is generally harmless. If the instrument be a little larger, there may be a path outlined in blood, but unless vital parts are penetrated no injury follows. That such punctures may, however, prove fatal is evidenced by the case, reported by Magnan,[2] of a woman who committed suicide by passing an ordinary pin, barely an inch and a quarter long, into the left side below the breast in the sixth intercostal space. On autopsy seven small punctures were found in the apex of the heart and the pericardium contained between 7 and 8 ounces of blood. If the instrument be of any size, such as a butcher's steel for instance, the wound presents a form quite different from that of the weapon. Instead of a round wound, we find a longitudinal lesion with two sharp angles and two sides of equal length, with little retraction of the edges. The direction of the long axis of such wounds varies in different parts of the body but remains uniform in the same part, their shape and direction being explained by the tension of the skin in the different areas. When the fibers of the skin follow different directions, the punctured wound may be irregular in shape and appear as if made by a triangular rather than by a round instrument. Further, as the direction of the fibers of the various tissue layers may be different, we may observe a different direction for each layer in case the wound is deep and involves such layers, as for instance in penetrating wounds of the stomach. Such wounds as the above "when large are smaller than the weapon, as the splitting of the skin has certain limits and also owing to the elasticity of the skin, which is put on the stretch by the weapon and relaxed on its withdrawal. When such wounds are small they are larger as a rule than the instrument causing them."[1]

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[1] See "Wounds" by Woolsey in *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 1907, **2,** 7.

[2] Compt. rend. de la Soc. de Biol., 1890, 9s. **2,** pt. 2. p. 35.

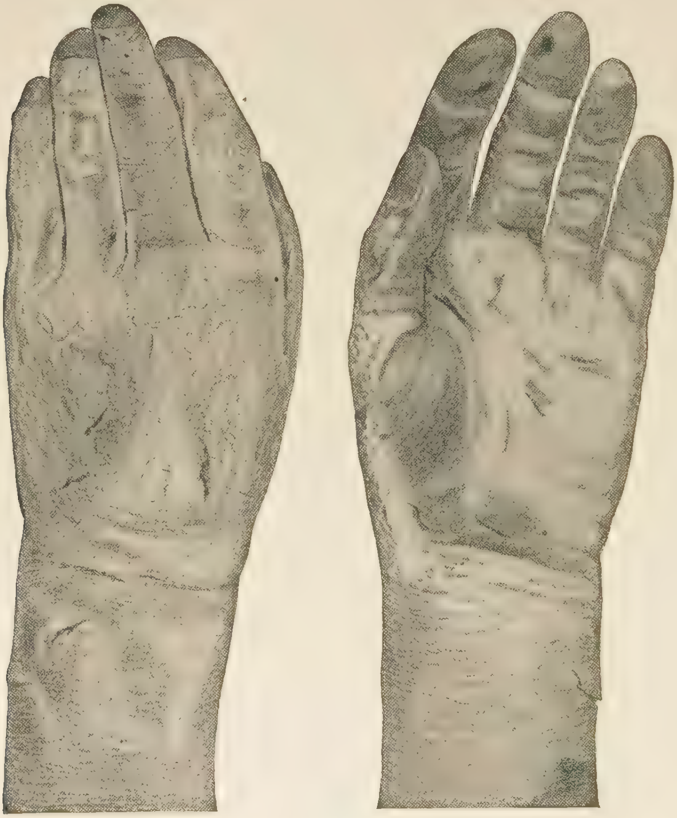

Fig. 12.—Punctured incised wounds of the left hand, made by a knife. (From Balch and Lewis, in Peterson, Haines and Webster, "Legal Medicine and Toxicology.")

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[1] See Woolsey, *Loc. cit.*, p. 11. Also, Fujiwara, Deutsche Ztschr. f. d. ges. gerichtl. Med., 1928, **12**, 65.

(*b*) *Wounds Made by Sharp Pointed and Cutting Instruments.*—If a punctured wound is made with a knife and the blow be perpendicular to the surface, the wound will have more or less the form of the weapon used, the margins being slightly concave and meeting at acute angles at the extremities. This is always the case if the knife be double-edged and is usually so if the knife blade has a broad back, although in the latter case the wound may occasionally be wedge-shaped. The depth of such wounds varies in different cases, equalling the length of the weapon or being less and, also, in some cases, being greater owing to the fact that the force of the blow may depress the tissues to such an extent that the point of the weapon reaches the deeper tissues.[1] Such wounds are often shorter and broader than the weapon, but usually are larger because the blow may be struck obliquely and there is some movement of the weapon in withdrawing it. If a stab wound pass through the body, the wound of entrance is usually larger than that of exit and the exit wound is usually everted, while the wound of entrance will also be everted if there has been rapid withdrawal of the weapon.

(*c*) *Wounds Made by Instruments with Ridges and Edges.*—Such punctured wounds are made by bayonets, foils, files, etc. If the point be sharp and the edges are cutting, the wound will present more or less the shape of the weapon, the edges of the wound corresponding to those of the weapon. If the edges of the weapon are not cutting, the wound will probably appear slit-like with the angles being unequal, or it may be stellate.

(*d*) *Wounds Made by Irregular Perforating Instruments.*—Wounds of this type do not indicate the character of the weapon used, as they may appear more like contusions although there is penetration. If the wound be made by sharp fragments of glass or crockery there is a combination of cutting and splitting of the tissues perforated. The margins of such wounds are jagged, irregular and contused.

3. Lacerated Wounds.—When the tissues are torn rather than cut the wound is called a lacerated one. These are produced by blunt or jagged instruments or object, such as stones, blunt weapons, crockery, obtuse-angled weapons or even by the teeth of one person striking against the body of another. Further, such wounds are not infrequently caused by falls against hard steps, frozen ground, ice, etc. Especially prone to show such lesions are the back of the head, the scalp over the eyebrows, the tissues over the malar bone, etc., and in such positions the wound may appear almost like an incised one, the force of the fall or a blow causing the bone to divide the tissues from within out, rather than from without in.

Lacerated wounds are usually irregular, jagged, torn and swollen. The skin in the region of the laceration is usually ecchymosed and the bones may be fractured, especially if they are near the surface. Such wounds are generally associated with but little hemorrhage, as the vessels are almost completely severed and the irregular edges facilitate clotting of the blood. However, if the blood vessels are only partially severed there may be considerable bleeding and blood may spurt some distance from the artery. Balch[1] records a case in which a man was struck by a thrown brick on the right forehead severing the anterior branch of the temporal artery, from which wound the blood spurted three and one quarter feet.

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[1] See Merkel, Deutsch. Ztschr. f. d. ges. gerichtl. Med., 1928, **12**, 137.

In these lacerated wounds it is a difficult matter to determine whether or not they were caused by a blow or a fall. The site of the wound may be of some aid in determining this point. For instance, if the wound is on the top of the head, a blow is more likely to have been the cause than a fall; however the presence of soil in the wound would tend to indicate the source as a fall rather than a blow. If the weapon alleged to have caused the wound fits into the wound, strong presumptive evidence is furnished, but it must be remembered that such wounds do not generally correspond in size or in shape to the weapon causing them. The weapon should be examined for blood, for hairs, and even for fibers from the clothing of the wounded individual.

4. Contused Wounds.—A *contusion* is a wound of living tissue produced by a blow of a blunt instrument, or by a fall or crushing without solution of the continuity of the external layers of the skin, although there may be a loss of continuity of the true skin or deeper structures. If this contusion be associated with a breach of continuity of the external surfaces, we have a *contused wound.* It would avoid much confusion if the term "contused wound" were not used as such, as most lacerated wounds are associated with some contusion and even an incised wound may, occasionally, show some contusion. We shall limit our discussion to contusions, simply recalling the fact that other types of wounds may show contusion and hence may, properly, be called lacerated-contused, incised-contused, etc.

Contusions (or bruises) are caused, according to our definition, by a blow of a blunt instrument or by a fall. The word instrument must not be interpreted as being simply some sort of generally recognized weapon, as it may be a stone, sandbag, club, fist, ball, iron bar, etc. These contusions usually involve a larger surface than do the other types of wounds mentioned, although they may be relatively small. In contusions there may, of course, be some excoriation of the skin, but there is no loss of external continuity.

The chief characteristic of contusions is the extravasation of blood into the subcutaneous tissues. Obviously, the amount of this effusion or *ecchymosis* will depend upon the force of the blow or pressure, the vascularity of the part involved, the texture of the tissues, and the condition of the vessels and the blood itself. It is well known that, in such conditions as scorbutus, purpura and hemophilia, bleeding is excited by the simplest procedures, so that a very extensive contusion may follow a slight blow or pressure under these circumstances. Redness appears first in the part to which the force is applied, and, in case the injury is slight, this redness may disappear within a few hours without any further change and without leaving any trace of the wound. However, with the harder blows or pressure, with which we are concerned, the subcutaneous tissues are crushed and blood is effused into the tissues from the ruptured blood vessels. Occasionally the contusion, if seen early, may have the shape of the vulnerating instrument, but after a time the swelling of the tissues prevents any such recognition. The initial redness of a contusion may soon become more dusky in hue, and then bluish-black, later green and finally yellow. The time at which the discoloration appears will vary to a great extent with the tissues involved: Thus, if there is firm resistance, as from bones, against which the force is applied, the discoloration may appear within 15 minutes to one-half hour, while, if the extravasation is produced in the deeper structures, the discoloration may not appear for one or two days later and then may appear at some distance from the point at which the force was applied. In the superficial ecchymoses the skin involved becomes swollen, the degree of this swelling depending upon the force applied and the amount of extravasation. In the deep-seated ecchymoses, as stated above, the discoloration may not appear for one or two days or may not appear at all. This late appearance of such ecchymoses must be borne in mind, as they may not appear until after death, so that confusion with post-mortem lividities may arise. The change of color tones in contusions are usually first apparent at the periphery of the wound, the fading of the color through the different spectral hues progressing from without toward the center of the bruise. However, as Glaister points out, it should be mentioned that in extravasations in the neighborhood of varicose veins, the change is first noticeable in the center. Just as there is a variation in the time of appearance of these ecchymoses, so we find that the time of disappearance will vary from a week to two or even three weeks, depending on the amount of extravasation and the rapidity of absorption.

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[1] "Homicide and Wounds" in *A System of Legal Medicine* by Hamilton and Godkin, 1894, I, 251.

It must be mentioned in this connection that very serious injury may be inflicted, and even death follow, without any external signs of contusion. This is especially true when the blow is landed or the pressure exerted upon yielding structures such as the abdomen. The wheel of an automobile may pass over a man's abdomen and rupture several of the internal organs without any appearance of ecchymosis, either ante or post mortem; a kick of a horse or a severe blow from a fist in a fight may rupture the bladder or intestine without any external signs appearing.

5. Gunshot Wounds.—Gunshot wounds are those caused by the forcing into or through the body of projectiles driven by the force of discharge of explosive material confined in a small space. While the ordinary firearms, such as the revolver, the automatic pistol, rifle, and sawed-off shotgun, are the weapons usually employed with criminal intent, yet we meet, especially in time of war, with wounds caused by the larger and more destructive guns. "Injuries, accidental, criminal, and suicidal, have been caused by explosives used in hollow castings, in gas pipe, large kegs with hollow ends, in bombs, and in almost any implement which, being hollow, permits of the use of the explosive force of powder or dynamite to cause injury or death." While, strictly speaking, wounds caused by bombs, etc. are not gunshot wounds, yet they come within the scope of our definition and will be so regarded.

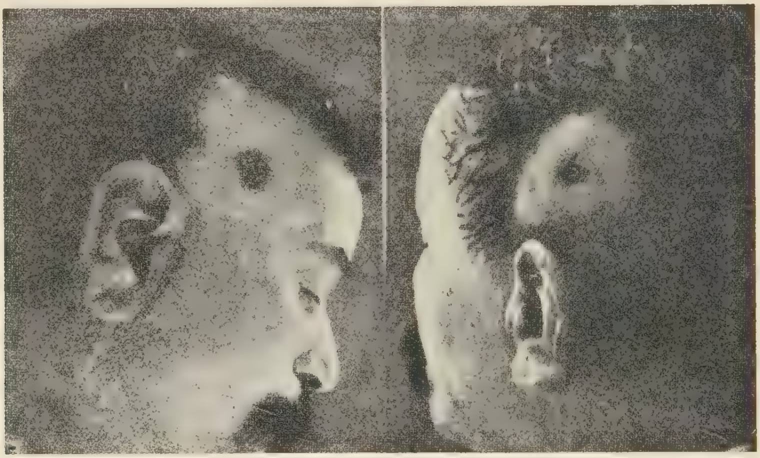

FIG. 13.—Entrance and exit holes of a 0.45 revolver bullet (suicide). Note the punched-in bruised appearance of the entrance wound and the torn everted appearance of the exit hole usually produced by a low-velocity bullet. Observe also the typical site and direction of fire usually found in suicide. (From Sydney Smith, "Forensic Medicine," J. and A. Churchill, Publishers, London.)

It is self-evident that the wounds produced by firearms will differ in appearance depending upon the type of weapon used, the size and type of projectile, the velocity of the projectile at the time it strikes, the force of the impact of the projectile, the distance of the weapon from the body, the angle at which the projectile is thrown, and the part of the body struck. It is impossible to discuss here such subjects as ballistics, trajectory or projectiles, or types of firearms, but it is to be said that these subjects may have an important bearing on many points which may arise in the medicolegal consideration of gunshot wounds.

Wounds produced by projectiles, which penetrate the tissues, may be contused or lacerated, or, if the modern steel-jacketed bullet moving at high velocity be the destructive agent, it may perforate the soft parts of the body with but a small wound of entrance and exit, the shape of the entrance wound being either circular or slit-like. As a rule the wound of entrance is about the size of the bullet, may have torn or contused edges, and its margins may be inverted[1]; while the wound of exit is usually larger than that of entrance, its edges are torn and somewhat everted, and the general explosive force of the projectile is more evident. If, however, the weapon be fired from a point very close to the body, the entrance wound is almost always greater than that of exit, owing to the laceration of the tissues by the gases of explosion. If the bullet strikes the body at an oblique angle, the entrance wound will be more elliptical in outline, and the skin will probably show a furrow or groove before the bullet actually penetrates. A soft-nosed bullet or even a steel-jacketed one moving at a low velocity may not have force enough to penetrate, when the wound is simply a contused one; while, if it still has power of penetration, it will produce a larger and more lacerated wound than a similar bullet moving with great velocity. If the weapon be fired nearly in contact with the body, the entrance wound is usually lacerated and the form of the wound is often cross-shaped. Glaister states that there are cases in which nothing more than contusion follows the firing of a revolver, whose muzzle is tightly applied to the skin of the body, a statement confirmed by Hall and Lewis.

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[1] See Pièdelièvre, Ann. de méd. lég., 1927, 7, 283.

It is to be remembered that a bullet in its flight may be deflected by striking some hard object, especially when it strikes a glancing impact. Sometimes bullets split into several fragments, causing multiple wounds. Revolver bullets may be deflected by almost any tissue of the body, unless they be the steel-jacketed bullets of the automatic pistol. Such soft bullets often flatten when they strike bones and are much changed in their course, while the steel-jacketed bullet is not usually deflected from its path, passing through bone or causing marked comminution or splintering when they strike. Glaister cites a case which shows the marked deflection, which a bullet may undergo, and the erratic course which it may take under such conditions. "The bullet first produced a comminuted fracture of the left thumb, which was in contact with the chest wall at the time, then entered the chest 2 inches above and the like distance to the inner side of the left nipple, passed upwards and outwards along the rib, was deflected downwards by the anterior edge of the left scapula, and continued on this course until it reached the crest of the left ilium; it then passed nearly vertically upwards to the wound of exit which was situated about 1½ inches below and in a line with the inferior angle of the left scapula. The pleura was wounded *en route*. After leaving the body of this patient it tore a large piece from the pectoral muscles of a child aged five, who was probably clinging to the old man from behind."[1]

The edges of the wound of entrance are commonly blackened by dirt or grease adhering to the bullet or by the lead from the bullet itself, but, if the projectile be moving with high velocity when it strikes, this blackening may not appear on the external wound, but will be visible in a perforated bone. Besides the above appearance, around the wound of entrance, in case the weapon be fired in close proximity to the body, there will be

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[1] See De, Indian. Med. Gaz., 1927, **62**, 479; Meixner, Arch. f. Kriminol., 1923, **75**, 81; Meixner and Werkgartner, Beitr. z. gerichtl. Med., 1928, **7**, 32.

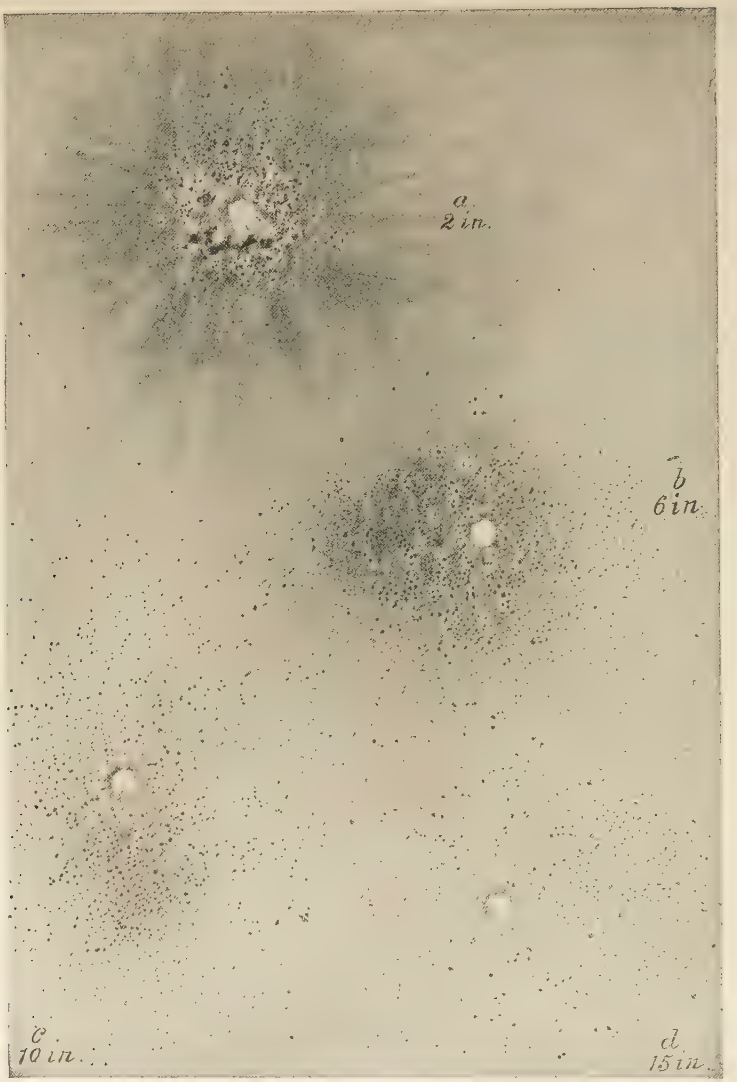

FIG. 14.—Brand and tattooing from .38-caliber Smith and Wesson revolver, Smith and Wesson cartridge, 4-inch barrel, white blotting-paper, as follows: *a*, Muzzle 2 inches from paper, sight upward (ordinary position); *b*, muzzle 6 inches from paper, sight held to the left (that is, the weapon was revolved one-quarter to left on long axis); *c*, muzzle 10 inches from paper, sight downward (pistol inverted); *d*, muzzle 15 inches from paper, sight held to the right. In *a* the whole field is smutted, brand above the bullet hole, powder marks distributed nearly equally about bullet-hole. Extensive firing of paper. In *b* brand shows to the left, less smutting, broader area of tattooing. In *c* brand shows underneath bullet hole, retreating from it. Still broader area of tattooing, more on side of the brand. In "*d*" brand has nearly disappeared, showing but slightly to the right. Tattooing still broader and more on side of brand. There was no fire to be extinguished except in *a*. (From Hall and Lewis, in Peterson, Haines and Webster, "Legal Medicine and Toxicology.")

observed an area of staining or blackening, the so-called *tattooing*, by the partially burned grains of powder thrown out with the bullet, and, also, more or less evidence of burning, the *brand* as this area is called, which is due to the gases of combustion. It should be remembered that the ammunition of automatic pistols and many rifles consists of smokeless powder, so that the tattooing will be more of a gray color and the burning will be less. Indeed, in some cases it will be necessary to examine the wounds with a hand lens in order to detect the grains of unburned powder, and, not infrequently a chemical examination of material from the edges of the wound may be essential in detecting traces of decomposition products of the powder.

It is a very difficult matter to determine the exact distance from which a gun was fired, as there are many circumstances upon which such a point will depend. As Hall and Lewis state: "Correspondence of holes in clothing with the wounds, and the carrying of fragments into the orifice, burning of the clothing or marking by powder grains, marking of person or clothing by wadding or by flame or powder grains, the finding of the ball in the body, the direction in which the periosteum, tendon, muscles, or other tissues about the wound are cut and the way in which the edges of the wounds in the skin are beveled all assist in determining the distance at which the gun was fired and the position of the gun when the bullet was discharged." At just what distances the tattooing and brand will result from the firing of a weapon depends upon the size of the weapon, its charge, and the quality of the weapon itself. To arrive at definite conclusions in any particular case, actual experiments with the suspected weapon or with one which is supposed to be similar to the one actually used should be made, as no two weapons will give the same results owing to differences in workmanship. Quoting again from Hall and Lewis: "Generally speaking, the tattooing and the brand will be the more distinct the less the distance of the weapon from the target, the heavier the weapon, and the better it is made. If the muzzle is held within an inch or so of the target there may be only burning about the edges of the bullet hole without distinct brand or tattooing, all being merged with the blackening about the edges of the orifice. The brand is generally not seen when the pistol is held at a distance exceeding a foot, and there are no powder marks beyond 2 to 3 feet. When the rifle or shotgun is used it is found at greater distances, depending upon the load, size, and caliber. At a distance several times that at which the brand is seen, tattooing is still distinct. The tattooing has very different limits than those of the brand. The latter is found only above the bullet hole, while the tattooing is found all around it, but more especially above. The brand is found immediately above the bullet hole when the weapon is fired at short range, and becomes farther removed as the distance is increased until it becomes too faint to be distinguished."[1]

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[1] "Gunshot Wounds" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, I, 340.

With the *shotgun* the wounds may differ somewhat in appearance from those just discussed. The load of a shotgun may consist of balls, fine or coarse shot, slugs, and other missles. At a close range, that is from one to 2 feet, the charge of a shotgun enters with a single point of entrance, although the wound is usually not round like that of a rifle or pistol bullet. As the distance increases the wound becomes more lacerated and separate holes may be seen around the border of the main wound. In some cases a single shot has struck the body and has caused death. Particles of the wadding or pieces of the paper shell may be blown into the body with the discharge. The tattooing and branding are apt to be more marked, as there is usually more unburnt powder and more flame with the shotgun than with the revolver or rifle. It must be mentioned that it is not necessary that a gun be loaded with any missiles to produce serious wounds, as powder itself and the wadding may prove very effective. It is not an uncommon thing to see wounds made by blank cartridges which are badly lacerated and which may be dangerous in themselves or become so from intercurrent tetanus infection. This possibility of wound infection must be remembered, as it was a more or less common thing to encounter cases of infection with various anerobic bacteria in the late war, the gas bacillus especially being carried into the wound by bits of clothing.

One of the most important questions which arises in connection with gunshot wounds is whether they are mortal or dangerous to life. It is self evident that such a question cannot be answered in general, but each case must be determined separately. The character of the weapon and its load, the part injured, the extent of the injury, the general health of the subject, and proper surgical treatment must all be considered. Many of these wounds are immediately fatal from shock or from hemorrhage, although immediate or extensive bleeding is not an inevitable result of such wounds. However if a large artery be severed, death will result from hemorrhage unless prompt interference is at hand. While many of the gunshot wounds heal promptly and leave no after effects, many of them are associated with a late fatal secondary hemorrhage or intercurrent infections may bring about a fatal result. It is to be mentioned in this connection that a surgeon when called to treat a case of gunshot wound must use reasonable care and skill in his handling of the case and, especially, must not do anything which might aggravate the condition unless he wishes to run the chance of a charge of malpractice. In this connection I quote from Park: "It is also held to be a violation of simple physiological and surgical rules to probe or carelessly search for a bullet whose location cannot be made out from a study of signs and symptoms in a given case. The act of probing breaks up blood-clots, often brings on fresh hemorrhage, is in a majority of cases unsatisfactory, frequently introduces specific elements from without, and really gives little, if any, more information than can be gathered from a study of the case without the use of the probe. If every bullet wound which did not call for immediate operation because of injury to some essential or vital part—such as a large blood vessel, or nerve trunk, or some of the viscera—were antiseptically and hermetically sealed at the very outset, there would be a much smaller percentage of death from gunshot wounds, either in civil or military practice, than now obtains. And it might be a matter upon which to go to the jury whether violation of such rules, to-day, does not mitigate the offense of the accused."[1]

In cases of violent death, however, in which a coroner's investigation is undertaken, it, often, becomes necessary to determine the course of the bullet as well as to obtain the bullet for evidence in court. In these days the study of various factors associated with ballistics is assuming great importance in forensic cases, as it is now quite possible to state, with almost certainty, that a given bullet found in the body of a person was or was not fired from a certain gun. This phase of the question, while of surpassing importance, can not be taken up at the present time, owing to the lack of space for proper elaboration. In some states, especially New York, Massachusetts, and Rhode Island, statutes have been enacted making it compulsory for physicians and superintendents of hospitals to report to the police authorities all bullet wounds, gunshot wounds, powder burns and other injuries caused by the discharge of a gun, pistol, or other firearm, and such bills are pending in Tennessee and Illinois[2]. While such bills are, undoubtedly, progressive and may greatly aid in the solution of crime, yet it would seem unjust to place the burden of making such reports only on medical individuals.

MEDICOLEGAL ASPECTS

Criminal, suicidal, or even accidental wounds, especially those resulting fatally, involve the medical practitioner or medical jurist in police or coroner's investigations or court procedure more frequently, perhaps, than any other cause. While the practitioner is not greatly concerned with the legal differentiation as to culpability for the causation of wounds and the different charges which may be brought against the one responsible for their infliction, yet he should realize the gravity of the situation confronting him when called to examine a wounded person or one recently dead from an inflicted wound. Professionally he is especially interested in his efforts to save life, to decide as to the seriousness of a given wound or wounds, or to determine the cause of death in any special case. Yet he must remember that his duties in such cases include, also, a more or less detailed examination into the possible source of the wound, the nature and extent of the wound, the condition of the wounded individual, and the careful study of the surroundings of the victim. His observations must be extensive and minute, and nothing should escape him, as he will be asked many questions, when on the witness-stand, that he cannot answer without a thorough knowledge of the situation. It has been said that "a medical man when he sees a dead body should notice everything," so that he should be forewarned when called upon to examine a person, either living or dead, who has recently been subjected to violence. If the individual does not die from the wounds inflicted, little legal action may arise, but this possibility can not excuse the examining physician from making a careful study of everything associated with the wounding. He must be on his guard as to his method of procedure and his surgical handling of the case, as the law demands the application of reasonable care and skill in the treatment and sound judgment as to conditions involved. Should the physician be careless and not exert his best care and skill, he lays himself open to the possibility of a charge of malpractice, and, further, may shift the burden of the causation of the death from the shoulders of a guilty criminal to his own, on the grounds that death would not have occurred had the surgical procedure been skillfully applied. Under such circumstances, there may arise the possibility of permitting a mitigation of the offense of the accused.

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[1] "Gunshot Wounds" in *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 2nd Ed., 1907, **2**, 171.

[2] See Editorial, Jour. Amer. Med. Assoc., 1929, **92**, 1603.

While it is not expected that a medical man will be familiar with the legal circumstances which render a wounding, in one case, justifiable, and, in another, criminal, yet it is well to have some idea as to the possible charges that may be brought against an accused, as intent plays a large role in the decision as to culpability and the physician may be able to point out, from his examination of the wounds and the surroundings, certain things which will be of importance in deciding the matter.

An unlawful attack upon the person of another is known in law as an *assault*. Any attempt or offer to do violence to another, coupled with the actual ability of the person to effect it, constitutes an assault, irrespective of whether the person is touched or not. Thus, the mere lifting of the fist or a cane, for instance, in a threatening manner, without any further effort to strike, constitutes an assault. In this connection it is to be recalled that a medical man may be open to the charge of an assault if he makes an examination of the genital organs of a female patient against her will, even though he be ordered by the court so to do. The unlawful beating or wounding of another is known in law as *battery*. The least degree of violence, or even touching another in anger or insolence, constitutes a battery. Hence, every battery includes an assault, but every assault does not cover a battery.

By *homicide* we understand the killing of a human being by a human being. In other words it is the destruction of a self-existent human life. Under this definition the destruction of an unborn child is, as we shall see later, not regarded as homicide, although it is criminal. However, it includes suicide and, also, death caused by culpable neglect. Homicide is divided, in law, into justifiable, excusable, and felonious.

Justifiable homicide proceeds from necessity, as where the proper officer inflicts capital punishment; where an officer of justice kills an offender who assaults or resists him and he cannot be otherwise captured; or where persons are killed in the dispersion of rebellious or riotous assemblies; or for the prevention of some atrocious crime.

Excusable homicide happens in consequence of misadventure, as where a man in doing a lawful act, without any intention of hurt, kills another by accident or in self-defense, or in defense of wife, children, parent, servant, etc. In connection with homicide in self-defense, it is to be pointed out that the person doing the killing must be in reasonable dread of death at the hands of another to warrant the action.

Felonious homicide covers both murder and manslaughter. By *murder* we understand the unlawful, premeditated, malicious killing of a human being by a person of sound mind, by an act causing death within a year and a day thereafter. It will thus be seen that the element of premeditated intent and malice play a large role in the interpretation of this form of homicide. Murder may be the charge instituted where death is due to personal violence, to poisoning, to criminal abortion, or to other causes, such as shooting in an attempt at burglary. By *manslaughter* is meant the unlawful killing of another without any malice either expressed or implied, which action may be either brought about by sudden passion or by improper action of another. The absence of premeditated malice in this form of homicide distinguishes it from murder. Included under the heading of manslaughter one would find such acts as using firearms in public streets and killing an individual; reckless automobile driving resulting in death of others; negligence in the performance of a lawful duty, as when a tower man on a railroad forgets to alter his signals, as a result of which deaths result. It is interesting to note, in connection with felonious homicide, that, where two individuals make a suicide compact and one dies and the other survives, the survivor is chargeable with murder; if a child die as a result of negligence of the parents in providing sufficient food or clothing, the parent is guilty of manslaughter, while if the negligence be intentional the charge is murder.

Examination of Victim and Surroundings.—When a practitioner is called to attend an individual, who has been wounded, his first duty is, of course, to his patient, although he is almost certain to become involved in a legal proceeding. He naturally makes his thorough physical examinations in order to determine the nature and the severity of the wound and then proceeds with his treatment, whether this be palliative or operative in character. In such cases, perhaps more than in any other type of case, the physician may be called upon to receive from the wounded individual what are called "dying declarations", which have been previously discussed.

If the victim die soon after the arrival of the physician or be dead when he is called, the duties of the examiner are shifted from those of a physician to those of a medical-jurist. In making his examinations, a minute investigation covering every possible detail should be made and extensive notes should be taken down as to the results. It is important in this connection that the physician remember that nothing should be disturbed, as far as the relations of the body to the surroundings and of things in the room are concerned, until the police or legal authorities arrive, as failure to observe this precaution has at times introduced many confusing complications into the solution of a crime. Everything in connection with the wound or wounds should be carefully noted, their situation, extent, direction, nature, whether incised, punctured, lacerated, gunshot, etc., all receiving close attention. The clothing of the wounded subject should also be carefully examined, especial attention being paid to the presence of holes or tears corresponding to wounds on the body, signs of blood stains, etc., as by such study many points may become clear. The presence of blood on the floor, ground, furniture, walls, etc., may give much information as to the nature of the wound, whether the victim moved after being wounded, and as to the suicidal or homicidal character of the wound. Evidences of a struggle between the victim and his assailant should be looked for, as this may have great bearing on the question of murder or suicide. The position of the body with relation to any weapon that may be found should be noted, and careful attention should be paid to the possibility of the presence of more than one type of wound, or the presence of fatal internal wounds, as the weapon found may not have produced all the wounds and, further, none of the wounds noted may have been sufficiently severe to have caused death. In other words, the physician should gather as much information as to the circumstances surrounding the death as is possible, as in this way he may be able to arrive at more definite conclusions, it being recalled that his own examinations of the wounds and the body and its surroundings may clearly controvert the statements made by others.

Evidence Furnished by Wounds.—In his examination of the assaulted or dead individual, the medical examiner should bear in mind that there are several possibilities with reference to the presence of wounds and their relation to the death. (1) There may be one wound or many and the question will be presented as to which of these, if any, have been the cause of death. It is to be said that the presence of many wounds is significant of murder, although it must be admitted that a suicide may wound himself several times and in different ways in order to make certain of the job, while in cases of accident multiple wounds are not uncommon. In this latter connection the type of wound and the location must be especially considered, as accidental wounds are rarely multiple where stab or gunshot wounds are concerned, although lacerated and contused wounds may appear on many parts of the same body. (2) There may be no external wound found, and yet the person may die from serious injuries. Thus, the passing of an auto over the abdomen of a body, the kick of a horse, or a blow from a fist may cause rupture of several of the internal viscera, without any external sign of violence. Further, marked injury resulting in death may be found in the brain as the result of violence applied through the ear, nose, or mouth, and no external evidence of such wounding be apparent. (3) There may be no wound, either external or internal, and yet death may result from criminal violence. A sudden blow on the epigastrium may cause death probably through paralysis of the solar plexus; death may be caused from fright bringing about syncope or shock as a result of a threatened assault; or there may be extravasations of blood in the brain from rupture of vessels as a result of very slight injury, although this may be criminal in character. (4) There may be many wounds on the body, some of them severe but not sufficient to cause death, and yet death occurs from other cause, such as the suicidal or homicidal administration of poison. For these reasons the examiner must be on his guard and make his final report only when he has made a thorough investigation as to the possibilities in the case and has arrived at a definite conclusion as to the actual cause of death.

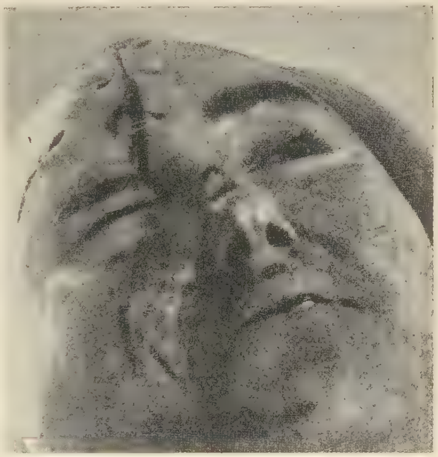

Fig. 15.—The two wounds, one over the right eyebrow and the other extending from the right orbit to the vertex, were both caused by a fall from a height. They, however, strongly resemble incised wounds. (From Sydney Smith, "Forensic Medicine," J. and A. Churchill, Publishers, London.)

1. *Character of the Wounds.*—The character of wounds, that is whether incised, punctured, lacerated, contused, or gunshot, has been previously discussed, so that we add here only a few points in relation to them. Wounds with clean-cut, sharply defined edges may usually be regarded as having been produced with a cutting instrument, but it must be remembered that sharp pieces of glass or earthen ware may produce similar wounds although these are usually somewhat more irregular in outline and partake, also, of the nature of punctured wounds. Glaister points out what he believes to be especially characteristic of wounds made by glass, namely, a parallelism of the edges of the wound, with a sudden inequality or tapering, sometimes to the form of a mere scratch, at one or other extremity. It is not an uncommon occurrence to note wounds over bony prominences, such as the forehead, zygomata, malar bones, jaw, etc., appearing as incised wounds, when the vulnerating force has been a blow with a blunt instrument or even a fall on a hard surface. As to punctured wounds there is little difficulty in determining their nature, but as to the exact type of weapon used it is not the simplest matter to decide. Much depends here on whether the weapon was used simply as a stabbing instrument or whether there were cutting edges and considerable movement was exerted in withdrawing the weapon. As pointed out previously, the wound usually has the form of the instrument

used, although at times the wound may appear slit-like, circular, or triangular from the same weapon. Lacerated wounds are produced by blunt instruments, but it must be remembered that the same body may show both lacerated and incised wounds produced by the same weapon, as when a bottle is used to strike the victim, the first wounds are contused or lacerated but may later appear incised, owing to the breaking of the bottle by the force of the blows. Ordinarily, contused wounds do not afford much opportunity of deciding as to the nature of the weapon used. All that can safely be said is that some blunt force was applied, although in some cases the clearly defined outlines of the instrument may be noticed. Where several wounds of the same type and general outline are found on the body, the possible evidence as to the weapon may be somewhat stronger, although it is very difficult to decide whether the contusion was the result of a blow with a weapon, with the fist, or was caused by a fall.

It must be repeated that it is not necessary to prove that a weapon was used in producing the wound, although much importance is attached to the finding of a weapon that might have been used. Wounding by whatever means constitutes an assault, the nature of which is determined largely by circumstances. The medical witness must not be drawn into stating too definitely that a certain weapon actually produced the wound in question. All that he is justified in saying is that it might or at least that the wound may have been caused by a similar weapon. Further, where no weapon is found, the witness should not attempt to describe too closely the weapon suspected of having caused the wound. As we have shown wounds may differ greatly in their appearance, even when made by the same vulnerating force, so that one is rarely in the position to affirm positively that such an instrument caused the actual wounds in question. Oftentimes a weapon may be found which seems to fit the wound exactly and yet it may have had nothing to do with the death. Thus Taylor[1] cites a case in which a woman was found dead in her room in the morning, and it was proven that she had fallen by accident on the highway the evening before. Death was due to fracture of the right parietal bone 4 inches in length. A man, who frequently quarreled with her, lived in the house in which the body was found and he actually let the woman into the house the evening before. In his room was found a hammer with two claws, which fitted into two indentations over the parietal bone. It was not until the adjourned inquest that the bonnet worn by the deceased woman was called for and examined. Two indentations were then found upon the back part of it, corresponding to those on the skull of the deceased. However, these indentations on the bonnet contained dust and dirt and rendered it probable that the fall in the road had really caused the fatal injury rather than a blow from the hammer in question.

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[1] *Medical Jurisprudence*, 12th Amer. Ed., 1897, p. 261.

A further point in connection with wounds and their relation to weapons is that it does not matter whether the wound was produced directly by a weapon or indirectly by any form of violence on the part of the assailant. Thus, a severe wound may be caused by striking a man with a weapon or by throwing such a missile as a brick and fracturing a skull, or the same wound may be caused by striking a man with the fist and knocking him down, thus causing him to fall against a brick. The actual wound here is caused by the brick, but its application is different in the two cases. In other words, guilt is determined by the act of violence and the intent back of this act, and not by the force used to produce the wounding.

2. *Situation of the Wound.*—The situation of a wound often affords considerable evidence as to whether the wound was homicidal, suicidal, or accidental. It is important that the exact location of the wound be noted by the examiner and that its situation in relation to known anatomical landmarks be determined. If there be more than one wound, the relation of each to the others should be noted and distances actually measured.

There are some parts of the body which either can not be reached at all or only with great difficulty by a person himself. For this reason we find that suicidal wounds are usually in the front part of the body or in those parts easily accessible. It is clear that any part of the body may be wounded by a second person, so that too much stress should not be laid upon the location of the wound as deciding the question of suicide or homicide. However, it is often possible to rule out suicide by a consideration of the location of a wound. The throat, chest, forearms, groin, etc., are usually selected by suicides when cutting instruments or penetrating weapons are used, while the chest over the heart, the mouth, or the temples are more frequently the site of suicidal attempts with firearms. Wounds of the back of the body are usually homicidal, although it must be admitted that they may be suicidal providing their direction is such as to permit of the possibility of the use of the weapon by the individual himself. Although the person, who has decided on self-destruction, usually adopts the methods which are obvious and which he believes will result promptly in death, yet there are many cases reported in which very unusual means are employed, so that we must not be misled by the type or situation of the wound. Contused wounds, especially those on the head, may be due to homicide, suicide, or accident. While the homicidal wounds may be on any part of the head, they are perhaps more commonly found on the top or the back, as the assult is usually committed from the rear. Suicidal head wounds are either on top or in front, while accidental head wounds usually appear on the vertex if the person has fallen from a height, or if caused by thrown projectiles or by a short fall they may appear in any situation. In regard to the situation of wounds and the relation to responsibility for death Taylor sums up the matter as follows: "There is no wound which a suicide is capable of inflicting upon himself which may not be produced by a murderer: but there are many wounds inflicted by a murderer which, from their situation and other circumstances, a suicide would be incapable of producing on his own person."

3. *The Extent of the Wound.*—The extent of the wound, that is the number and importance of the parts involved, has much to do with questions of immediate death and, also, with a decision as to the type of crime committed. The dimensions of each and every wound on the body should be accurately measured, their shape, form, and, where possible, their depth being determined. While incised wounds of the neck are more commonly suicidal in nature, yet murderers at times resort to this method of producing death, or produce such wounds on the victim previously killed by some other means. In suicidal cut-throat the incision is usually regular in appearance, does not usually involve the structures on both sides of the neck, and seldom reaches far enough to involve the posterior structures, yet there are many cases in which the muscles and vessels on both sides of the neck are divided. While regularity of the wound is presumptive of suicide, yet it must be said that a murderer might inflict such a regular cut on the throat of a sleeping or intoxicated person or on one incapable of resistance. As a rule, however, homicidal incised wounds of the throat are irregular and jagged, owing to the resistance of the individual attacked. Multiple stab wounds of the chest may be either suicidal or homicidal, the suicidal wounds tending to be limited to a more or less circumscribed area, while the homicidal wounds are widely distributed as a rule. Not infrequently the peculiar form of a wound or its location and extent may lead to suspicion of homicide against certain individuals, as, when wounds of the throat resemble those made in cutting the throats of animals, a butcher might be suspected. Occasionally wounds found on the hands of the dead individual may have some presumptive value in deciding as to suicide or homicide, as the person attacked ordinarily attempts to protect himself with his hands and, in so doing, may receive such additional wounds.

4. *The Direction of the Wound.*—The direction of the wound often enables a decision to be formed as to the suicidal or homicidal origin. Incised wounds of the throat, of suicidal origin, usually run from left to right in a horizontal or oblique direction, owing to the fact that most people are right-handed. Where the incision runs oblique, the beginning of the cut is at a higher level than its end. Of course, if the person attempting suicide be left-handed, the incision will run in a direction from right to left. In suicidal punctured wounds the direction is ordinarily from right to left and from above downwards, while with such homicidal wounds the direction may be either from right to left or left to right and from below upwards or above downwards. It is to be remembered, however, that homicidal wounds, whether incised or punctured, would have the same direction as suicidal wounds providing the assailant stood behind his victim. With gunshot wounds it is some-

what more difficult to determine the direction as the bullet is so frequently deflected by the tissues that its course is very irregular. Multiple wounds are probably more indicative of homicide than of suicide, the direction being usually the same in each wound in case of suicide, while in homicide the direction may vary as the assailant changes his position. In the case of such multiple wounds, the examiner will be called upon to state which, if any, are mortal and which wounds were first produced. Further, it is to be remembered that several different weapons may be used, either in suicide or homicide. The suicide may stab himself, then shoot himself and finally hit himself over the head with a hammer, while a victim may be attacked by several different assailants.

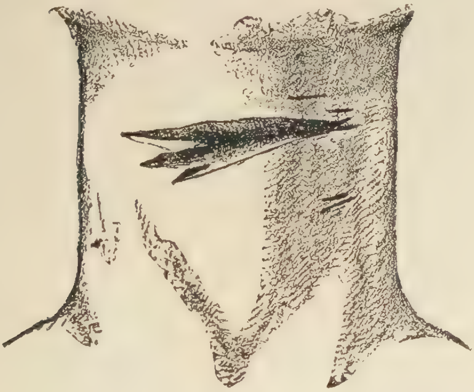

FIG. 16.

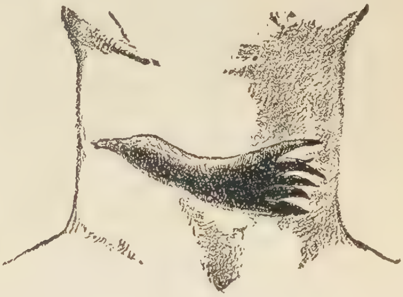

FIG. 17.

FIG. 16.—Suicidal cut throat from left to right, showing the tentative cuts at the commencement and the serrations at the termination of the wound. (From Witthaus and Becker "Medical Jurisprudence, Forensic Medicine and Toxicology," Wm. Wood and Co., Publishers.)

FIG. 17.—Homicidal cut throat from right to left, showing a tentative cut at the commencement and the serrations at the termination of the wound. (From Witthaus and Becker, "Medical Jurisprudence, Forensic Medicine and Toxicology," Wm. Wood and Co., Publishers.)

With accidental wounds the direction has little meaning, except in so far as the surrounding circumstances may point to the accuracy of the conclusions that death was accidental or that the direction of the wound was such that it could not have occured from the weapon in question. In some cases, however, more or less difficulty may arise in deciding the matter. As Taylor remarks: "But if the position of the deceased with respect to surrounding objects has been disturbed; if the weapon has been removed, and the body carried to a distance; then it will not always be easy to distinguish a wound accidentally received from one inflicted by a suicide or a murderer."

5. *Which of the Wounds are Mortal?* The subject of the nature of wounds has been previously discussed. It is clear that wounds differ

as to their danger, depending upon the parts involved and the extent of the injury inflicted. It is not within the scope of this work to discuss all types of fatal wounds, suffice it to say that wounds of the heart and of the large vessels, wounds of the respiratory organs, and wounds of the brain and cord usually prove fatal, unless prompt and radical surgical intervention follows. So, also, extensive wounds of the internal viscera may prove promptly fatal unless given immediate attention. It must be mentioned that a wound that completely and promptly disables one person, may not have the same effect on another. Penetrating wounds of the heart are usually fatal, but death may not occur for some hours and the individual may be able to perform many voluntary acts before death, as in the case cited by Baltharand[1] of an Italian laborer who lived 16 hours after inflicting upon himself a stab wound 1 cm. long outside and 2 mm. inside, situated 6 cm. from the apex of the heart. A further case[2] is that of suicidal penetration of the heart, 2 cm. from the apex, by an aluminum pipestem, death following not until 8 days after the penetration. Also, in gunshot wounds, in which important arteries are laid open, the individual may be able to walk quite a distance before collapsing from the hemorrhage. The medical examiner must, by his dissection, trace the course of each wound in order to determine just what organs have been injured and how extensive the damage is. Having made such investigations, he is in a position to determine whether any of the wounds were mortal. In this connection, it must be repeated that, even though he finds mortal wounds of certain organs, the examiner must be certain that no natural cause of death is present. It is not an infrequent occurrence for a medical witness to be asked on the witness-stand in connection with a suspected murder, whether or not he made a complete examination of the body to determine the presence of natural causes of death. If he has not done so, doubt may be cast on the point of the wounds causing the death. Further, the possibility of a person having taken poison and then being wounded must be remembered, as there are many recorded cases in which the poisoning actually caused the death, although severe wounds were present on the body and were reported as the fatal cause. The investigations must, therefore, be sufficiently extensive to permit the examiner or others associated with him to determine just what was the cause of death and which wound was the mortal one.

6. *Was the Wound Inflicted before or after Death?* This question is possibly a resultant of the previous one. It is not unusual to find cases in which poison, for instance, has been administered from which the subject dies and subsequently wounds are inflicted by the poisoner in order to direct attention from the actual cause of death. So, also, cases are reported in which fatal wounds have been inflicted, and after death the murderer has inflicted other wounds, which in themselves

[1] Ann. de méd. lég., 1928, **8**, 117.

[2] Hunter, Staub and Lunsford, Arch. Path., 1928, **6**, 807.

would have been fatal had they been produced during life, in order to direct the attention of the authorities to possible suicide.

Wounds inflicted during life and proving fatal within a few (10 to 12) hours have the characteristics mentioned under the previous discussions of character of wounds. These are as follows: If the wound be an incised one, the edges will be sharply cut and everted, there will be considerable hemorrhage, generally arterial in nature, and much diffusion of blood into the surrounding muscular and connective tissues, and clots of blood will appear within the wound. Of course, if there be no wounding of blood vessels, there may be little evidence of bleeding, but the edges of the wound will be everted and the skin retracted. Punctured and lacerated wounds may show much hemorrhage, if made during life, although in some of the most extensive wounds of this type, the hemorrhage may be slight, but clots of blood will be found adhering to the separated parts. With contused wounds, there is swelling, infiltration of the effused blood into the surrounding tissues, gradual change of color through violet, blue, green to yellow.

If the wound is made on the dead body there will be little or no bleeding, or if there is it is entirely venous in character, there is an absence of clots in the wound or tissues, there is no diffusion of blood into the surrounding cellular tissue, and the edges of the wound are not retracted or everted. In the contused wounds on the dead body, there is no swelling, practically no blood is effused, there are practically no clots, and there is no change in color. Post-mortem lividities have at times been confused with ecchymoses made before death, but such a mistake should not occur. In the lividities, there is no elevation of the livid area above the skin, the location of the lividities is in the dependent parts of the body, and when incised no effused or coagulated blood escapes.

While wounds made before and after death have the characteristics mentioned, it must be recalled that molecular death is not coincident with somatic death, so that so long as body heat, fluidity of the blood, and contractility of the skin and muscles are present, wounds will have the appearance of those made during life. Hence one must be guarded in his statements as to the infliction of the wounds before or after death. All that one is warranted in saying is that a given wound must have been inflicted either during life or immediately after, that is within ½ to 2 hours as a maximum, as Christison has shown.

Evidence Furnished by Circumstances.—While perhaps strictly speaking the evidence, derived from the circumstances under which the body of a wounded person may be found, is more especially associated with the efforts of the police to unravel the cause and source of the death, yet many of these circumstances are such that the medical examiner must know before he is in a proper position to bear just witness as to the facts in the case. The examiner should be cautious in drawing inferences and should not permit the conditions to prejudice him against any party as the possible criminal. All of the points involved are certain to be brought out at the trial, or the coroner's inquest, and the medical examiner is the one most likely to observe them, as he is usually the first one called to the scene of the death. In his investigations, however, it is important that he disturb nothing until after the arrival of the authorities, but he may, of course, examine the victim in order to arrive at a conclusion as to the actual presence of death.

1. *The Position of the Body.*—The position of the body when found and its relation to its surroundings may give some information as to the manner in which the wound was inflicted. Thus, if a body is found leaning on a desk with a bullet wound in the back, it is evident that the bullet was fired while the individual was seated at his desk; or if a body be found in bed with the throat cut and the hands are beneath the bed clothes, there is strong presumptive evidence of murder. The direction of the wound may indicate the position the body was in when the wound was inflicted, or may show the relative positions of the victim and his assailant. In some cases the position in which the body is found is explicable only on the basis of homicide, although occasionally the wound may be suicidal or accidental and the wounded individual may have fallen into a position of very unusual nature. The fact that individuals, who have received fatal wounds, may walk some distance or perform other acts should be remembered, as this may account for the finding of the wounded person some distance from the place of the wounding. Of course, it is possible that a murderer may move his victim from one place to another, but under such circumstances the condition of the clothing and possible blood spots along the trail may furnish a clue to this action. The actual position of the dead body should be carefully noted in its relation to surrounding objects and to windows and doors, and, especially, as to its relationship to pools or clots of blood, in order to permit of some deduction as to whether the body had been moved after falling. If a weapon be found, the relation of the position of the body to that of the weapon should be noted, so that the possibility of suicidal or accidental death may be considered. It is well under all these circumstances to make diagrams or drawings of the position of the body in relation to the various objects in the room, as many points arising in the legal investigation may be explained by later study of these.

2. *State of the Clothing of the Subject.*—It is wise and, indeed, necessary to examine the clothing of the victim in order to determine whether there are any marks of the passage of a weapon or of a projectile through the different layers. Should any such holes or tears be present, they should be compared with the wounds on the body before any clothing is removed. If the clothes are not to be kept intact, the portions containing the cuts or holes should be cut out and preserved. Close inspection of the clothing should be made in cases of possible gunshot wounds, in order to determine the presence of burning and deposition of powder grains in the fabric, as such indications furnish much evidence as to

the distance from which the shot was fired. Further, note should be made as to any disordered state of the clothing, as this is suspicious of a struggle and, therefore, of homicide, although it is possible that a suicide may have disarranged his clothing in his last efforts. The presence of blood on the clothes should be looked for, and the exact location of any spots carefully noted.

3. *The Position and Nature of the Weapon.*—If a person has died from an accidental or suicidal wound, within a relatively short time, the weapon is usually found close to the body or a very short distance away. Under such circumstances the exact location with relation to the body should be noted, the side of the body on which it is found, whether it has the appearance of having been laid down or dropped or thrown, whether the blade is open (if it be a knife), and whether or not there are signs of blood upon it. It is to be remembered that a suicide may throw the weapon some distance after inflicting a fatal wound, or he may even hide it, in order to give the impression of a homicide instead of a suicide. In many cases, however, the weapon is found tightly grasped in the hand of the deceased. This is probably the best bit of circumstantial evidence in favor of a suicide, as it is impossible for the murderer to place the weapon in the hand of his victim and have the weapon so tightly grasped as it is by the hand of a suicide. If the weapon be found in such a position, it should be carefully examined for traces of blood and, if a firearm, for evidence of recent firing.

If the weapon be found at a distance from the body, or if it cannot be found at all, the evidence points to homicide, although, as stated above, the suicide may throw the weapon or, even, conceal it. Under such conditions, the other circumstances in the case must be considered before giving an answer as to the possibilities in the case. Wherever the weapon be found, it should be closely inspected to determine its characteristics, whether sharp or blunt, straight or curved, if a firearm whether recently fired, or if a bruising instrument, whether there is evidence of blood or hair upon it.

As regards the question as to the recent firing of a gun found at or near the scene of the crime, much may be learned from a careful inspection and chemical examination of the firearm, the conditions varying, of course, with the type of powder used in the shell. The first thing to do in examining a firearm is to note whether or not there is any smell at the muzzle end, and, if so, its nature and intensity. Following this, the color of the interior of muzzle end should be noted. The breech should then be opened and a small amount of water poured into the barrel and allowed to run into a receiving vessel, in order to wash out the deposits on the inside of the barrel. The deposit at the muzzle end of the gun is, in the case of black powder, generally black, but sometimes dark gray, the intensity of the color gradually changing in time, so that the stains may be light gray or even white. "The solution obtained by washing out the barrel with water immediately after firing contains black particles in suspension, is of a greenish or yellowish color, smells of sulphuretted hydrogen, is alkaline and contains sulphide, sulphate, no nitrite or nitrate, but sometimes a trace of ferrous iron. If various intervals of time, gradually increasing in length, be allowed to elapse before the barrel is washed out, the suspended matter, which is black at first, finally becomes grey or brown, while the solution gradually loses its green or yellow color, and becomes colorless or brown. The sulphide disappears, but the alkalinity, sulphate and iron remain, and a little nitrite develops. The suspended matter at first contains iron in the ferrous condition, but later part of the iron is in the ferric state."[1] As the solid products of combustion of black powder are, for the most part, potassium carbonate, potassium sulphate, potassium sulphide, potassium thiosulphate, and potassium thiocyante, it follows that any or all of these compounds may be detected in the products washed from the gun barrel. While free hydrogen sulphide may be detected at the muzzle end of the barrel, if examination be made very soon after the gun is fired, it is rather rare that such is found in the usual police examinations, as too much time elapses before the chemist has opportunity to make his investigation. The most of the potassium sulphide disappears in 5 to 6 hours, although a trace may remain for a longer period. The sulphate, which is apparently present from the first in traces, gradually increases in amount as time elapses. If the sulphide has disappeared, the thiosulphate may be detected. The alkalinity is due to the presence of carbonate, which gradually changes to the bicarbonate, so that the degree of alkalinity diminishes in time. Smith[2] states that "in twenty-four hours there is about twice as much carbonate as bicarbonate; this gradually changes, and in about seven days the bicarbonate greatly exceeds the carbonate." With the nitro powders, the nature of the solid products formed vary with the composition of the powder. Sulphuretted hydrogen and sulphides are not present, the reaction is neutral, instead of alkaline, and nitrite and nitrates are usually present in appreciable amounts, while sulphates are found only in traces.

If the bullet be found in the body of the victim, it is important, in some cases, to determine, if possible, whether or not it might have been fired from the weapon found at the scene of the crime. It will be remembered that the rifling of the gun barrel has certain characteristics as to number and direction of the grooves, depending upon the make of gun. As the bullet passes through the barrel it receives impressions of these grooves and, also, marks of any irregularities in the specific gun barrel. This leads to the possibility of determining whether a certain bullet has been fired from a certain gun, by comparison of these grooves and markings, with those made on similar bullets fired from the same gun by the investigator. These marks really have the same significance in this respect, as the examination of finger prints has, inasmuch as no two guns, whether of the same or different makes, have exactly the same markings, and the bullets fired from them will, also, vary. This study of ballistics can not be discussed here, but it is to be said that it is yielding much information in criminal cases.

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[1] Lucas, *Forensic Chemistry*, 1921, p. 155.

[2] *Forensic Medicine*, 2nd ed., 1928, p. 176.

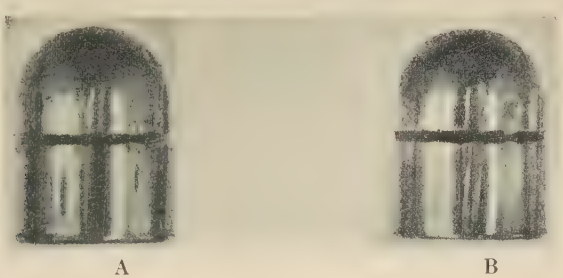

Fig. 18.—Bullet A was extracted from the body of a man murdered in 1920. Bullet B was fired from a Webley revolver (.455 inch) seized in 1926. The markings are identical, and indicate that the seized revolver was the weapon used in the crime. (From Sydney Smith, "Forensic Medicine," J. and A. Churchill, Publishers, London.)

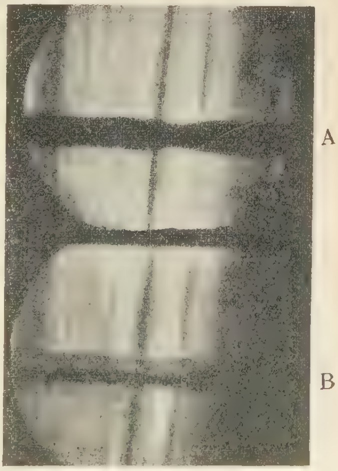

Fig. 19.—A more highly magnified photograph of one of the grooves and portion of the surface of the bullets figured in Fig. 18, to show the identical nature of the markings. (From Sydney Smith, "Forensic Medicine," J. and A. Churchill, Publishers, London.)

With reference to the presence of blood upon a weapon it is to be said that there may be much, little, or none. With the instruments causing contusion, there may be no blood at all, unless there have been repeated blows or the first blow caused much laceration. A long-bladed knife may show very little blood, owing to the fact that it is plunged in rapidly and withdrawn quickly and is wiped off to a great extent by the skin as it is withdrawn, or, if made through the clothing, these will remove most of the blood. About all that one will find on the knife in such cases is a slight, thin, yellow coating. If the knife be short, blood will, probably, show on or near the handle, in the notch for opening the blade, or in the letters stamped on the blade. It is to be remembered that, in cases of homicide, the murderer may have washed the blade thoroughly so that nothing will appear. Further, it is not an infrequent occurence for the assailant to make his attack with one weapon and then substitute one belonging to the victim, in order to make the death appear suicidal. Under these circumstances the blade of the knife will not, in all probability, fit the wound, or it may not be such as could have inflicted the wound in question; if it be a firearm, the caliber may be different from that of the bullet in the body, or the comparison of the grooves and markings on this bullet with those on bullets fired from the gun by the investigator will not agree. It is to be said, in this connection, that different bullets fired from the same gun will not, except in most rare cases, show exactly the same markings, as the scratches and erosions on the gun barrel change with each firing, but the grooves will accurately correspond in slight faults in one or more grooves and in secondary markings between the grooves.

If death be due to the use of bruising or even of cutting instruments, the weapon should be examined for the presence of hair or other substances as well as blood. Should any fibers be found, these should be closely examined and the fact determined that they are hair, or fibers of wool, cotton, linen, etc., as this will throw light on the question of whether this weapon may have been used in the assault, especially if it can be determined that the hair corresponds to that of the victim or that the other fibers are similar to those of the clothing or hat worn by the deceased.

While the examiner will, of course, attempt to determine whether any weapon found in the neighborhood of a dead body might have been associated with the death, and will in his investigations try to fit the weapon into the wound in order to establish such possibilities, yet he must, as previously stated, be very guarded in saying that a given weapon produced a given wound. All that he is justified in saying is that it might have done so, or that a similar weapon caused the wound in question.

4. *The Surroundings of the Wounded Individual.*—In making an examination of the surroundings, in cases of death from wounding, one of the first things to be determined is whether the body has been moved after being found. If it has, much of the evidence to be gained by the study of the surroundings will be questionable. It is, of course, perfectly possible for the wounded person to move around to quite an extent after receiving a fatal wound, so that the room should be examined thoroughly with reference to blood stains on the wall, furniture, floor, etc. If the person has fallen motionless after receiving his wound, there will probably be considerable blood in the region of the body and about the person and clothing. Under these conditions, evidence of an attempt on the part of the murderer or others to move the body will be shown by a bloody trail. The furniture, walls and floor should be examined for evidences of a possible struggle. Any circumstances, however minute, should be noticed as these may play a large rôle in the solution of the problem.

5. *Presence of Blood.*—In examining the person of the victim and his clothes, one will always find blood in case the wound be such that external bleeding has occurred. Of course, there are many fatal wounds that are not associated with external bleeding, so that under these conditions

no stains would be expected. A thorough examination should be directed to all articles in the neighborhood of the victim, a good light being necessary for this purpose. The number of blood spots to be expected will depend on the nature of the wounds inflicted and the amount of spurting of blood from severed arteries. If blood be found on the walls, floor, or furniture, the position of these spots with reference to the body should be accurately noted, their shape and size should be observed, and their state, that is whether fluid or coagulated, should be determined, as these will all throw light on the type of wound inflicted and, also, on the position of the body when wounded. Any bloody finger or foot prints should be examined closely, in order to determine whether or not they might have been made by the wounded individual or his assailant. If the finger prints show the papillary ridges, impressions of these should be made and preserved for comparison with those of the deceased or his suspected assailant.

It not infrequently happens that, in the struggle at the time of the wounding, or by blood spurting from the wound, or by touching the wounded individual, the clothes or the hands of the assailant are stained with blood. However, it is to be remembered that the natural direction of spurting blood is away from the hand holding the weapon, so that it may be possible for the assailant to avoid contamination. Moreover, criminals not infrequently remove their clothing before committing a crime or cover their outer clothing with overalls, which they later hide or burn. Thus, Courvoisier, who was convicted of the murder of Lord Russell, admitted that he wore no clothes when he committed the murder. However, it is wise in all cases to examine the clothes of any suspected assailant in order to determine the presence of human blood, but it must be remembered that blood is not infrequently found on the clothing of perfectly innocent persons.

Are the Wounds Homicidal, Suicidal, or Accidental? The determination of this question may be considered to belong, more properly, to the legal authorities than to the medical jurist, but it is to be said that the evidence of the medical examiner may be absolutely necessary in the solution of this question. While it is not to be expected that the general practitioner will be in a position to observe all the points which we have discussed relative to wounds and the evidence to be obtained therefrom, yet he should make his observations as extensive as possible in order that he may be in a position to answer intelligently questions put to him. Of course, one skilled in such investigations will go even further than we have outlined, so that he will be able, in all probability, to give a more or less decisive answer to the question at issue.

We shall not attempt to enlarge our discussion as to the points involved in this question, as we have discussed under the various headings the conditions under which the wound may be regarded as coming under one or another of the captions of homicide, suicide, or accident. Every possible point in connection with the body of the dead individual, with the wounds in question, with the weapon involved if any be found, with the surroundings of the dead person, and with any outside circumstances that may come to light, will have to be investigated and studied closely before any answer may be attempted, and, even then, one may have to be very guarded as to his conclusions. Never take anything for granted in connection with a wound, but determine every point that many have a bearing on the case.

REGIONAL WOUNDS

Space does not permit the inclusion in this discussion of the special wounds and injuries of various parts of the body. It has been stated that any portion of the body may be the site of a wound and the type of the wound, in relation to the part injured, will determine the severity of the wound. Fractures of the skull constitute a large proportion of the wounds for which the surgeon is called, and the close study of such lesions leads to many interesting medicolegal conclusions. Extensive discussion of the wounds of the head, thorax, abdomen, and other parts of the body is given in all works on surgery and in the larger books on medical jurisprudence, so that we must content ourselves with reference to such sources with the statement that the medicolegal phases of such wounds do not differ, in any essential detail, from the points already discussed with relation to wounds in general.

CHAPTER IX

EXAMINATION OF BLOOD STAINS

As stated in the preceding chapter, blood stains on the body of a wounded individual, on his clothing, or on the furniture, walls, floor in the locality of the body, on the weapon, or on clothes supposed or known to belong to the suspected assailant, are of great importance in connection with the solution of various crimes. Everything that is any way suspicious should be taken for examination.

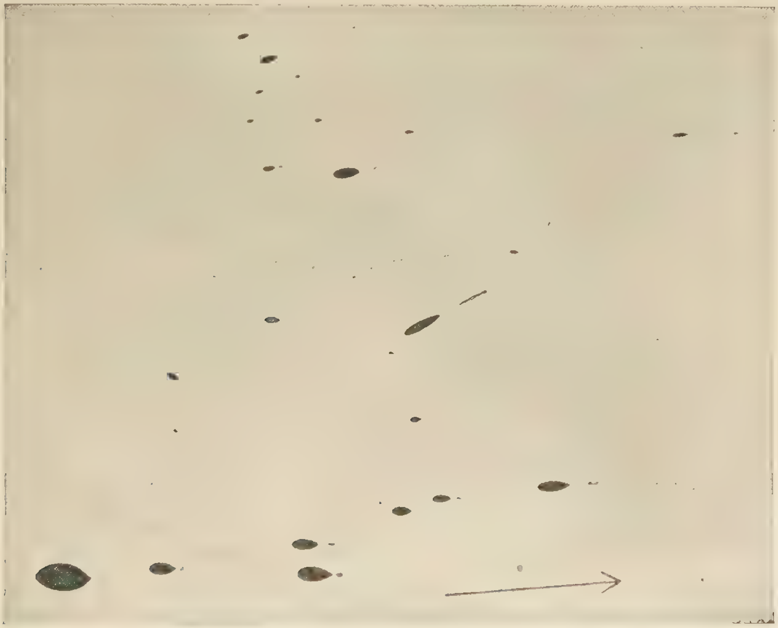

FIG. 20.—Showing direction from which the blood came. (From Hektoen and McNally, in Peterson, Haines and Webster, "Legal Medicine and Toxicology.")

If the suspected articles are not collected at the scene of the crime by the one who is to examine them, a condition which usually prevails in medicolegal investigations, they should be preserved in such a way that their identity can not be disputed and they should be recorded as having come from a definite source, so that the examiner may have the proper data for his records. These articles must be kept intact and under observation or under lock and key until turned over to the expert by a responsible associate of the legal authorities. It often happens that such articles are sent to the expert by express. If such be the case it is important that the sender take a receipt for the package from the express company and demand a return receipt from the consignee, in order to preserve the direct line of communication. The examiner receiving the specimens from the authorities, either by direct transmission or through the medium of express or registered mail, becomes responsible for preserving their identity. He will, of course, keep all such specimens under his personal observation or under lock and key and not permit others to have access to them, as he alone is responsible for them.

It often happens that the examiner is called in at the time of the original investigation and, under such conditions, he will collect the specimens himself, making his notes as to all the conditions which have been previously discussed. The form of the blood spots found on walls, floors, clothing, etc. usually gives a definite idea as to the direction from which the blood came. When blood spurting from an artery strikes a surface obliquely, it forms an oval or pear-shaped stain, the base being nearer the source and the bulk of the blood being driven toward the stem end, the length of the stem or narrow end indicating the speed of the impact. If the surface against which the blood strikes be vertical, the blood will flow down till it clots, the lower portion being thick and the upper part broad and thin. However, if the surface against which the blood strikes be rough, coagulation occurs quite promptly so that there is little running down of the blood. If the blood be dropped onto a perpendicular surface, especially if this be smooth, it tends to spatter more or less, the shape of the spot and the amount of spattering depending upon the height from which the blood falls. These points will, of course, be noted by the examiner at the time of collection of his specimens.

GROSS EXAMINATION

Before beginning his detailed technical examination of the suspicious spots, the examiner should make a preliminary examination of all articles submitted to him, making his investigations both with the naked eye and with magnifying glasses in both daylight and artificial light. Each article received should be carefully described and should be thoroughly examined for the presence of blood spots. In the case of clothing, the examination should cover both the outside and inside, special attention being directed to the seams and insides of pockets. If any suspicious spots are found, these should be closely described and their exact location relative to definite points should be determined by measurement. The shoes are very often neglected in such examinations, but frequently they afford valuable information, especially the soles, insteps and laces. Weapons are very important in this connection, although it must be remembered that there may be no blood stains on the actual weapon used in the assault. However, it should be a working rule never to discard an article until certain that there are no stains or suspicious material upon it. If any spots are removed from the articles submitted their exact location should be noted and the statement made that the whole or part of a definite spot was taken for examination.

It is not necessary to discuss the physical and chemical properties of blood in detail, as we are not concerned with many of these factors. However, there are some points, in connection with the changes which blood undergoes after being shed, that must be discussed briefly, in order that we may be able to understand the variations in appearance of blood stains after being exposed to the elements for some time and being subjected to extremes of heat and cold.

1. Coagulation of Blood.—When blood is drawn or flows from the vessels of the body, it separates after a time into two portions, a solid mass known as the clot (coagulum or crassamentum), which is red in color and contains the corpuscles of the blood, and a slightly yellowish fluid, the blood-serum. Normally, human blood begins to clot in two to three minutes and is completely clotted in seven to nine minutes. The blood of animals clots in a shorter or longer time depending upon the animal. In man, the time of coagulation varies in some pathological conditions, being lessened in some and increased in others. There are, however, certain conditions which have to do with the blood after it is shed that may increase or decrease the period of coagulation. Thus, coagulation is hastened by increase of the temperature between 37° and 50° C. (while heating to 56° C. destroys the power of coagulation); by exposure of a large surface of blood to the air; by contact with rough surfaces; by being agitated or stirred; and by dilution with less than twice its volume of water. Coagulation is delayed by exposure to cold; contact with oily, waxy, or syrupy substances; and by addition of certain chemicals, as potassium oxalate or sodium citrate.

2. Drying of Blood.—This process is quite independent of coagulation and is not part of the same process. The time required for blood to dry has some importance in determining the possible age of the stain. Blood dries more slowly than water owing to its viscous character. "The character of the surface on which the blood falls also has considerable bearing on the time required for the complete drying of the blood. If the surface be an absorbent one, so that the blood may permeate the substance itself, as in the case of a piece of unstarched cotton or linen cloth, the drying takes place quite rapidly, but if the surface be a non-absorbent one, like that of a piece of glass or a board having a smooth surface, and also in the case of some kinds of dense woven fabrics, the time required for the drying of a drop of blood is much greater than that of a drop of water of equal size."[1] From experiments made by Wood it seems clear that from one to two hours is required for a single drop of blood to become dry, while larger amounts dry much more slowly.

When blood is completely dry, it is stiff and brittle, so that clots and stains often have a scale-like appearance if on non-absorbent surfaces. If the dried blood be upon cloth, the stained area will appear more or less stiff. While it is possible to remove much of such stain from soiled clothing or clothes by washing, yet this process makes the stain more diffuse and seldom removes every trace of the blood. This point should be remembered, as it is possible to detect blood in washed clothing, unless this process has been extremely thorough.

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[1] Hektoen and McNally, "Medicolegal Examination of Blood and Blood-Stains" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 898.

3. Color of Blood Stains.—While arterial blood is bright red and venous blood dark crimson, the difference can not usually be determined in a dried stain. While most people are familiar with the color of blood when dried, yet it must not be assumed that the color of a stain is an infallible guide, as the color of the blood stain may show many shadings, varying from brown to orange, light yellow, pink, greenish or even black, depending upon circumstances. Further, there are many substances, which might form stains on various articles, that may be confused with blood stains, if naked-eye appearances are made the test of differentiation.

A fresh blood stain usually has, under ordinary circumstances, a fairly bright scarlet color. On exposure to daylight and air, the color gradually changes to a dull brown for about ten days, when the color may remain more or less permanent, although on much longer standing it may become almost black. If the stain be in the direct sunlight, the change to brown will be much quicker and, if on thin fabrics like linen, the color may be a gray shade instead of brown. Besides direct sunlight, the application of a high degree of heat or treatment with alcohol, gasoline, or formalin will change the color to brown, or deepen the color of the stain rapidly. It is evident, therefore, that it is a difficult matter to state the probable age of a blood stain from a consideration of its color alone. About all that one is justified in saying is that the stain is fresh blood, or one made within a period of about ten days, if the color is relatively bright; while, if the color be brown, the age is indefinite. Exposure to sunlight, action of heat and cold, rain or snow, and effect of chemical agents must all be taken into consideration before any statement as to age should be ventured.

It is to be stated that one should not assume that a given stain is due to blood, simply because it is red or brownish. On the other hand, the examiner should not neglect to examine stains, because they do not look like blood to him. Various fruit and vegetable coloring matters, aniline dyes, iron rust, paints, spots of lemon or orange juice on steel, fecal matter, highly colored urine, and oftentimes, tar, pitch, and grease may cause stains that may confuse the examiner and must be differentiated from blood. The addition of ammonia water to the aqueous or saline extract changes the reddish tint of vegetable or fruit stains to a green, crimson, or blue-black tone, while blood pigment is unaltered; the stains of aniline dyes that might resemble blood become yellow on the addition of nitric acid, while blood does not show this change; iron rust and red paints dissolve in warm hydrochloric acid and give a blue color with potassium ferrocyanide or a red color with potassium sulphocyanate;

the lemon or orange spots are soluble in cold water forming a light yellow solution, having an acid reaction and showing the tests for iron; fecal matter and urine are best detected by microscopic examination of the scraped material; while tar and pitch dissolve readily in turpentine or alcohol, neither of which solvents affect blood; and the grease is detected by placing a piece of blotting paper over the stain and pressing a hot iron over it, or the grease stain may be dissolved in ether, gasoline, or chloroform. It is seen, therefore, that the confusing substances do not react like blood and will not show the reactions which are more or less characteristic of blood. However, the possibility must be remembered that blood stains may be found overlying or mixed with stains from any of the above substances, so that reactions for blood may be obtained even under circumstances that do not appear at all favorable.

4. Solubility of Blood Stains.—It is clear that the solubility of blood or a blood stain will depend upon its age, the material upon which it is found, and its degree of exposure to the elements and possible treatment with chemical agents.

With reference to the age of the stain in relation to solubility it is to be said that the fresher the stain, the greater and more rapid is its solubility. Fresh stains are readily soluble in distilled water or in physiological salt solution. The older the stain the more difficultly soluble it becomes in the menstrua mentioned, so it may be necessary in some refractive cases to use other solvents, although water or salt solution are the agents of choice when possibly applicable. As the age of the stain increases, the oxyhemoglobin is changed to hemoglobin, then to methemoglobin, and finally to insoluble hematin.

Pfaff[1] has attempted to determine the relative age of blood stains by noting their solubility in dilute aqueous solution of arsenous acid (1:120). Fresh blood dissolves in a few minutes; blood 1 to 2 days old, in 15 minutes; 3 to 8 days old, in 30 minutes; 2 to 4 weeks old, in 1 to 2 hours; 4 to 6 months old, in 3 to 4 hours; and blood a year or more old, in 4 to 8 hours. While the above findings of Pfaff may be used as a working basis, yet it will be found in some cases that the results are more or less unreliable, owing to alterations in the solubility of the blood pigment on aging.

If the stain has been exposed to heat or chemicals, the extraction with water or salt solution requires a long period and even then may not be successful. Much depends, of course, on the type of test that one is using to determine the presence of blood, as to the effectiveness of a solvent. Katayama[2] found that blood stains, dried in porcelain dishes and exposed to a temperature of 80° C. for an indefinite period or to 100° C. for an hour, was soluble in distilled water in 24 hours; while if heated to 120° C. for one hour the stains were soluble in 24 hours in strong solution of potassium hydroxide or in glacial acetic acid, or a week in ammonia water, cyanide of potassium, or dilute sulphuric acid and alcohol; while if heated to 140° C. for 1 hour, the stains dissolved only in strong potassium hydroxide or in glacial acetic acid. Hammerl found that heating the stain to 135° to 143° C. prevented the guaiac reaction and, if heated to 145° C., Teichmann's test was usually negative. Sutherland, however, was able to obtain Teichmann's crystals from stains heated to 140° C. for two hours and extracted either with glacial acetic acid or with concentrated sulphuric acid. Mirto reports that blood heated to 120° C. for 1 hour, 130° C. for 30 minutes, or to 150° to 160° C. for 10 to 15 minutes is still soluble in normal salt solution and responds to the precipitin test, while Ferrai could not obtain this reaction with stains heated to 130° C. for 1 hour, 140° C. for 20 minutes, or 160° C. for 5 minutes. Pisani[1] advises the extraction of the stain with 50 per cent potassium hydroxide and the treatment of this extract with a saturated solution of ammonium sulphate followed by shaking the mixture with a little pyridine, by which treatment the hemoglobin is broken up, the globin salted out and the hematin extracted by the pyridine. By evaporation of the pyridine, the hematin is left behind and may be identified by Teichmann's hemin crystal test. It is well to remember, as stated by Ewing[2], that concentrated sulphuric acid will always extract pigment from heated stains, and this solution will always give the spectrum of hematoporphyrin. If all other solvents fail to give solutions that show the presence of blood by the usual tests, then resort should be made to the use of concentrated sulphuric acid.

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[1] Vrtljschr, f, ger. Med., 1862, **21**, 266.

[2] Vrtljschr. f. ger. Med., 1888, **49**, 269.

The usual articles upon which blood stains are found are cloth or clothing, wood, plaster, metal and leather. Stains on cloth usually yield, at least in time, to extraction with salt solution or distilled water. However, in dyed cloths, the mordants may so fix the blood that solution is very difficult, especially when the cloth has been ironed, has been washed with soap and water, or has been cleaned with gasoline or benzene. In such cases, digestion of the cloth either in a dilute solution of citric acid or ammonia will usually result in solution. As we shall see later only certain solutions are applicable when the study of the corpuscles is undertaken or when attempts are made to obtain the specific biological test, but where the chemical or spectroscopic tests are involved the point at issue is to obtain a solution of the coloring matter of the blood, so that we must use such solvents as will accomplish solution. If the stain be on plaster, it is scraped off and treated with the same solvents used in dissolving stains from cloth. Stains on leather or wood, especially oak or elm, are sometimes refractive to solution in water or salt solution, owing to the fact that the tannic acid forms a compound with blood that is difficultly soluble. In such cases, if solution is not effected with the usual solvents, extract the stain with a 2 per cent. solution of hydrochloric acid as recommended by Sorby. Stains on weapons, especially very rusty ones, sometimes do not yield to the solvents readily, owing to the fact that rust is insoluble and may so cover up the particles of blood that solution is not accomlisphed. Under such conditions scrape the rust from the surface of the weapon by means of a clean instrument and pulverize it very finely and then extract in the usual way.

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[1] Arch. farmacol. sper., 1928, **44**, 260.

[2] See *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 2nd Ed., 1909, **3**, 816.

With stains that are relatively fresh, a portion of the stain should be scraped off on to a piece of clean white paper, or, if the stain be on cloth, a portion of the stained as well as the unstained part of the material is cut out. This suspected material is then placed in watch glasses or in small test-tubes and about 1 çc. of the solvent added. Allow the preparations to stand for some time in order to effect the solution, noting from time to time whether or not any color is present in order that you may have some general idea as to the age of the stain. When the coloring matter of the stain has passed into solution, you are ready for the identifying tests.

METHODS OF IDENTIFYING BLOOD-STAINS

The methods employed in detecting blood are chemical, spectroscopic, microscopic, and biologic. The chemical and spectroscopic tests are used to determine the presence of hemoglobin or its decomposition products, but as yet no difference is established in hemoglobins of different origin. The microscopic examination is employed for the detection of the red blood corpuscles and for the classification of the animal from which the blood came. The biologic test, decides, at least within narrow limits, the species of the animal from which the blood came, that is determines whether the blood is human or otherwise.

Chemical Tests.—Having obtained a solution, preferably in water or physiological salt solution, of the stain in question, there are certain tests which are applied as preliminary ones, but which must not be regarded as definitely indicative of the presence of blood. These tests, if resulting positively, indicate that blood *may* be present, while, if a negative result is obtained, blood may be assumed to be absent, unless the stain is one that is so old or so altered by exposure to weather or to chemical action or to high temperatures that it is insoluble in the menstrua used. Under these circumstances, reliance will probably have to be placed upon the spectroscopic tests.

1. *The Protein Test.*—As blood is an albuminous fluid containing a coloring matter, in the body of the red cells, which is itself a chromoprotein, it is to be expected that an aqueous extract of such material will contain protein. Such solutions, depending upon the amount of hemoglobin present, are more or less reddish in color. If such a solution be heated to the boiling point, preferably after very slight acidulation with acetic acid, the red color of the solution is quickly lost, the fluid becomes more or less cloudy, and gradually a dirty-gray or brownish

precipitate settles out, due to the coagulation of the protein of the solution. If a few drops of sodium hydroxide solution be added and the mixture shaken, the precipitate dissolves and the liquid shows a more or less red color by reflected light and a greenish tint by transmitted light, the so-called dichroic reaction.

While the immediate discharge of the red color of the solution and the formation of a precipitate or turbidity on heating, distinguishes blood from the red extracts of fruits, vegetables, flowers, and dyes, yet it must be said that the same coagulation of protein will occur from any albuminous fluid, such as milk, pus, sputum, nasal discharge, etc., any one of which may become contaminated with red coloring matter and dry upon clothing or other material. For this reason the above test is not in any way distinctive of blood, but indicates simply that the stain contains a red coloring matter and protein material, both of which exist in blood.

2. *Oxidation Tests.*—Hemoglobin has the power of combining with oxygen to form a loose combination known as oxy-hemoglobin, from which oxygen is set free when the oxygen pressure is reduced. For this reason hemoglobin acts as an oxygen transferer, a property which may be utilized in testing for its presence by means of certain oxidizable substances, which yield definite colored compounds. While so-called oxidases, found to a more or less extent in all animal cells, may, also, produce this oxidation, yet it is to be remembered that the action of the true oxidases is destroyed by heating the solution to boiling, while hemoglobin is unaffected by such a proceeding. For the purpose of determining this oxygen-transferring power of hemoglobin or its derivatives, guaiac resin, benzidin, and phenolphthalin are probably the most satisfactory, although many others have been advocated.

(*a*) *The Guaiacum Test.*—This test is known as van Deen's, Day's or Schönbein's test. It is performed by transferring a small portion of the stain or a small bit of the stained cloth to a small porcelain dish and adding a few drops of water to dissolve the blood pigment, the amount of time necessary to accomplish this depending upon factors previously discussed. To this watery extract are then added a few drops of freshly prepared tincture of guaiacum and the mixture is closely watched to see if there is any trace of a blue color formed. When the guaiac tincture is added to the watery extract there is always a whitish turbidity noticed, due to the insolubility of the resin in water. If no blue color has been observed at this time, a few drops of hydrogen dioxide are added, when a beautiful blue color will appear almost at once in the presence of blood. Whether the stain is fresh or old, or whether concentrated or much diluted, this test produces a blue color. However, it is important that the blue color be produced *only* after addition of the hydrogen dioxide, as the blue color with the guaiacum alone is useless as an indication of blood. This blue color is due to the oxidation of the guaiac resin to guaiaconic acid and then to guaiac blue.

A very good method of performing this test is that advised by Taylor of adding a drop or two of water directly to the stain *in situ* and allowing this to remain for a few minutes, after which a piece of filter paper is pressed down upon the moistened spot. The addition of the tincture of guaiac and the hydrogen dioxide is then made to the extract on the filter paper, a blue color indicating the possible presence of blood and a negative test practically proving the absence of blood, although reservation must be made for the cases in which the blood pigment may have been destroyed as previously indicated.

This test is a fairly delicate one, showing the presence of blood pigment in a solution of 1 to 5000 according to Wormley.[1] Taylor[2] was able to obtain a positive reaction from stains 24 years old found on a towel, so that it is possible by this test to detect old stains, especially when they have not undergone decomposition. It is to be said, however, that the value of this test is greater in its negative phase than when positive. If one obtain negative results, especially when the stains are fairly fresh, he may be almost certain that no blood is present, but, if his results be positive, he must consider the possibility of other substances being present. In other words, this test must be confirmed by other tests, which indicate blood somewhat more definitely. It has been found that many other substances will produce a blue color with the guaiacum test. Thus, manganate and permanganate of potassium, peroxide of manganese, peroxide of lead, chlorine, bromine, iodine, nitric and chromic acids, ferric chloride, ferric sulphate, iron alum, ferro- and ferricyanide of potassium, cupric sulphate and nitrate, indigo, gum acacia, gluten, unboiled milk, raw potato pulp, pus, sweat, and any living cell or its intracellular enzymes react positively. Hence, it will be seen that caution is necessary in the proper interpretation of this test.

(*b*) *The Benzidine Test.*—This test is a much more delicate one than is the guaiacum test. It is performed as follows: A small portion of the stained area is cut from cloth, or, if the stain be on a hard object, a small fragment is scraped off and placed in a shallow porcelain dish or white tile and over this are poured a few drops of a freshly prepared mixture consisting of a saturated solution of benzidine in alcohol or glacial acetic acid with an equal volume of hydrogen peroxide. In the presence of blood a greenish-blue or a pure blue color will appear almost immediately. Increasing the amount of peroxide increases the sensitiveness of the test, while the depth of color may be increased by adding more benzidine. Lucas[3] states that the addition of a few drops of pyridine to the stained material before the addition of the benzidine solution promotes rapidity of action.

This reaction will detect blood when present in a dilution of one part in 300,000 or even somewhat higher. It reacts with old stains and, on account of its delicacy, is more reliable in the negative phase, as well as in its positive, than the guaiacum test. Lucas reports that "An instantaneous reaction is given by blood stains which have been kept in a semi-tropical laboratory for eighteen years. Blood boiled for an hour, and kept for thirteen years acts readily. Blood stains on rusty iron kept for four years react within five seconds. It is almost impossible to wash out blood from cloth so that the fabric will fail to give a blue colour with the reagent." The chief value of this test is in showing the absence of blood, as the same oxidizing agents, oxidases, and peroxidases mentioned previously react with this test. Boiling the solution to be tested will remove from the field of action the oxidases or peroxidases.

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[1] *Micro-Chemistry of Poisons*, 1885, p. 710.

[2] Guy's Hosp. Rep., 1867, **13,** 431.

[3] *Forensic Chemistry*, 1921, p. 22.

(*c*) *The Phenolphthalin Test.*—Phenolphthalin is a product of the reduction of phenolphthalein by zinc in alkaline solution. When oxidized in alkaline solution, it is converted into phenolphthalein with production of an intense red color. Phenolphthalin may now be obtained in the market, and may be used directly in the production of the reagent, unless it shows a slight reddish tint when it may require purification by crystallization from water and alcohol.

The reagent for the test may be prepared as follows: Dissolve 0.032 gram of phenolphthalin in 21 cc. of N/10 sodium hydroxide solution and make up to a volume of 100 cc. with redistilled water. In the absence of a delicate scales, one may proceed as follows: Mix a slight excess of phenolphthalin with 1 cc. of N/10 sodium hydroxide solution, add 10 to 20 cc. of redistilled water, shake thoroughly and filter. To the filtrate add 20 cc. of N/10 sodium hydroxide solution and make the mixture up to 100 cc. with water.

In performing the test proceed as follows: To 1 part of the aqueous extract of the stain add 2 parts of the reagent and 1 or 2 drops of hydrogen peroxide. Within a few minutes a deep purplish-red or pink color will be obtained if blood be present, the depth of color depending on the amount of blood pigment present. A control test should be made by replacing water for the extract of the stain and adding the other reagents in the same manner, when no coloration or at most only a very faint pink will be obtained.

This is probably the most delicate test at our disposal for the detection of blood, as its limit of delicacy seems to be about 1 part of blood in 8 million of water, although Kastle has detected 1 part in 80 million. The reaction is retarded, according to Kastle, by the extracts of various animal tissues or various secretions of the body. For this reason we are never able to detect as small amounts of blood in the secretions as in the watery solutions, which concern us in medicolegal cases. Boiling the solutions to be tested destroys the oxidases and peroxidases. Owing to the delicacy of this test care should be taken to exclude extraneous factors before venturing an opinion as to the positive presence of blood in medicolegal cases. Here, a negative result is almost conclusive as to the absence of blood, or at least it does not exist in a form soluble in the solvents used.

3. *The Teichmann or Hemin Test.*—This test is the most important one for detection of blood pigment, is very delicate, and has the advantage that a positive result is definite proof of the presence of blood. The test is usually performed as follows: A small portion of the dried blood is scraped from the surface of the stained area and placed upon a glass slide. If the stain be a diffuse one or has soaked into cloth, a portion of the stain may be scraped off as a dust-like material, or preferably, a few fibers of the stained area are teased out on the slide. The material on the slide is then covered with a drop or two of a very dilute (0.01 per cent.) solution of sodium chloride, and the fluid evaporated to dryness at a low heat. A few drops of glacial acetic acid are then placed upon the salted stain and the preparation is covered with a cover glass. Now slowly evaporate the glacial acetic acid by holding the slide above a flame in such a way that the solution steams and bubbles of gas are noted, indicating that the acid is heated to the boiling point. As the acid evaporates, more is allowed to run in under the cover glass and the heating to incipient boiling is repeated. Allow the slide to cool and examine under the high dry power of the microscope. If blood be present, one will observe long, narrow, dark brown, rhombic plates, which appear singly, in cross-shaped formation, or in sheafs or rosettes. These crystals are chloride of hematin and are called "hemin" crystals. If the blood be difficultly soluble, as in cases when the blood is old or has

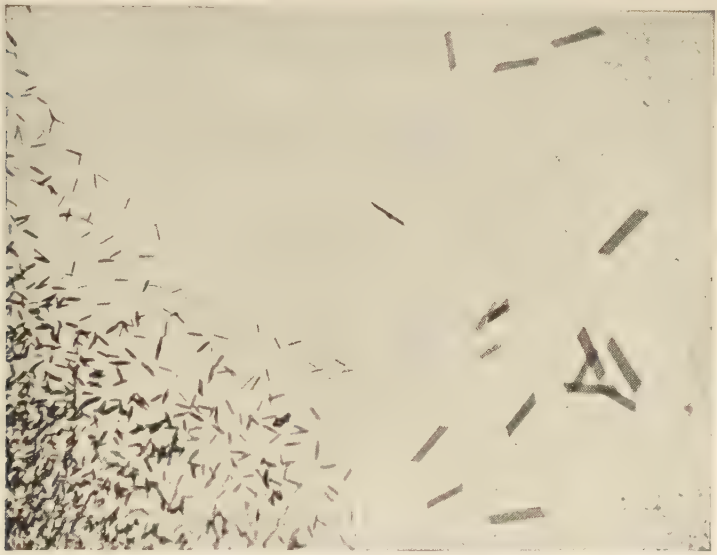

FIG. 21.—Hemin crystals obtained in two tests for blood by Teichmann's method. Note the great difference in size of crystals formed under slightly different conditions (photographs, × 250). (From Todd and Sanford.)

been heated, the rhombic crystals are as a rule much shorter and broader and may appear somewhat irregular as, for instance, dumb-bell or whetstone-shaped crystals. In many preparations, especially if the boiling has been very prolonged, the crystals will appear just beyond the edges of the cover glass, where they have been carried by the evaporating acid.

This test is not always successful, owing to the fact that the slide may have been overheated, that the salt solution added to the stain may have been too concentrated, or that the stain is so old or so altered by chemical agents that no crystals are formed. It is essential for success that the salted stain be dry before the acid is added, the glacial acetic acid must be anhydrous, and, possibly the most important, the slide must not be heated to *brisk* boiling. It is important that the crystals have a distinct yellow to chocolate-brown color. Colorless needles of sodium chloride may be confusing, if this color tone of the hemin crystals be overlooked, and, further, one often observes long, narrow, rhombic plates of a *blue* color, but larger than those of hemin, in cases in which the stain is removed from indigo-dyed cloths.

In case the blood stain is very diffuse owing to the fact that attempts have been made to wash it from the cloth, it is occasionally wise to concentrate the material as follows: Cut out a considerable portion of the cloth and place in an evaporating dish containing distilled water with a small crystal of sodium chloride or iodide. Soak the cloth for some time, pressing it occasionally with a glass rod, remove the fluid, and extract again. Filter the combined extracts, strongly acidify with acetic acid and add a few cc. of saturated solution of sodium tungstate, which has also been acidified with acetic acid. A light-colored precipitate will form, if blood be present, and this may be rendered more flocculent by boiling. Filter, wash with water, and dry. This material may be used for the oxidation or hemin tests and will probably give somewhat more distinct results owing to the concentration of the material. Spectroscopic tests may, also, be made with this material as will be later discussed.

Beam and Freak[1] have advanced a method for obtaining hemin crystals, which obviates the possibility of overheating and too rapid evaporation of the acid as well as the interference of the protein material of the blood with the crystallization.

The technic of this test is as follows: A small quantity of the suspected material is placed at the bottom of a flat arsenic sublimation tube about 6 by 3 mm. and 35 mm. long. A few drops of glacial acetic acid containing from 0.01 to 0.1 per cent, sodium chloride are added and a very fine cotton thread adjusted so that its upper end is near the top of the tube and the lower end reaches to the bottom of the liquid. The thread should be everywhere in contact with the tube, to which it adheres readily by being moistened with the liquid. The tube is now placed in a rack and allowed to remain until crystallization has taken place. The clear acid solution of the blood gradually passes through and along the thread, being drawn up by capillary action to the mouth of the tube. Evaporation of the acid takes place very slowly and is complete only after 12 to 24 hours. The crystals usually begin to appear on or near the upper half of the thread in about an hour and may be recognized by the low power of the microscope, and ultimately become so large that they may be readily seen with a hand lens.

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[1] Biochem. Jour. 1915, **9**, 171.

Spectroscopic Tests.—The evidence furnished by the spectroscopic examination of blood stains is quite exact. The method requires only small amounts of material and is applicable not only to hemoglobin itself but to all of its decomposition products. The basis of the test is, as is known, the appearance of characteristic absorption bands in the visible spectrum formed by light passing through solutions of blood pigments or even through solid material containing these pigments.

Hemoglobin is the red coloring matter of the blood, being found in the blood of all vertebrates except *amphioxus* and *leptocephalus* and, also, in that of many invertebrates. The pigment found in fresh blood is ordinarily that of oxyhemoglobin. On standing until it dries and, especially, when it is exposed to an atmosphere containing products of combustion of coal or is exposed to the action of direct sunlight for some time, hemoglobin changes into methemoglobin. If the stain is kept in a damp place, or is exposed to long-continued heat, or is decomposed by chemical action, the pigment present is hematin; while, if the stain be acted upon by such agencies as remove the iron, hematoporphyrin will be found. There are other compounds of hemoglobin, such as nitric oxide hemoglobin, carbon monoxide hemoglobin, and sulph-hemoglobin, which have medicolegal importance in connection with poisoning from certain substances, but none of these latter compounds have a place in the discussion of identification of blood stains and will be left for later treatment.

Where there is a large amount of blood or stain available, it is a simple matter to obtain sufficient amount of the solution to permit of the use of the usual large spectroscope, when the work of identification is possibly easier. However, in the ordinary medicolegal cases the amount of material at hand is not large enough for this purpose, so that resort is had to the smaller direct-vision spectroscope or, where such is available, to the micro-spectroscope, which is fitted directly to an ordinary microscope.

Method of Examination.—As previously mentioned, the pigment present in a blood stain depends upon many circumstances and may consist of oxyhemoglobin, methemoglobin, or hematin. If the material be plentiful, and the stain relatively fresh, dissolve a small portion of the stain in water or physiological salt solution and examine directly with the spectroscope, placing the solution in a small tube or chamber with parallel sides, so that the rays of light may pass directly through, adjust the light so that the spectrum is clearly visible and study the location of the absorption bands. If the bands of oxy-hemoglobin be found, add to the solution while it is in the chamber a drop or two of a reducing agent, such as ammonium sulphide or Stokes' solution[1], and stir. If this mixture be now examined spectroscopically, the spectrum of hemoglobin will be observed. It is important that this change of oxyhemoglobin to hemoglobin be obtained, as in this way differentiation is possible from certain spectra, which may resemble that of oxyhemoglobin but which are not due to blood, and, it may be said in passing, that this procedure serves to distinguish carboxyhemoglobin from oxyhemoglobin and is of importance in the diagnosis of carbon monoxide poisoning.

If the stain is an old one or has become partially decomposed, the spectrum of methemoglobin will probably appear, instead of that of oxyhemoglobin. If the stain is so old or has been so changed by action of heat, light, or chemicals that it yields no color to the water, it should be extracted with a little dilute sodium hydroxide solution, when the resulting solution will show the absorption spectrum of hematin in alkaline solution. If ammonium sulphide or Stokes' solution be added to this solution, the spectrum now changes to that of hemochromogen. If one use glacial acetic acid, instead of sodium hydroxide, on these old stains, the solution shows the spectrum of hematin in acid solution. If the stain prove refractive to all of the above treatments, then it should be treated with concentrated sulphuric acid, which will dissolve it with a purplish-red color, the solution showing the spectrum of hematoporphyrin in acid solution.

Oxyhemoglobin.—A dilute solution of oxyhemoglobin shows a spectrum with two absorption bands between the Fraunhofer lines D and E. One band, α, is narrower but darker and sharper and lies on the line D, the other, β, is broader, less defined and less dark and lies close to E. As the dilution becomes weaker the band β first disappears. With increased concentration the bands become broader, the space between them smaller and the blue and violet parts of the spectrum darkened. Attempt should, therefore, be made to make such a dilution as will show the two typical bands of oxyhemoglobin. In practice this can be done only by subsequent dilutions of an original solution, if the bands appear to coalesce.

Hemoglobin.—The solution of hemoglobin in water is more violet or purplish than one of oxyhemoglobin of like concentration. Such solutions of hemoglobin absorb the blue and violet rays of the spectrum to a less marked degree than do those of oxyhemoglobin. In proper dilution a solution of hemoglobin shows a spectrum with one broad not clearly defined band, called γ, between D and E., lying toward the red end of the spectrum a little over the Fraunhofer line D.

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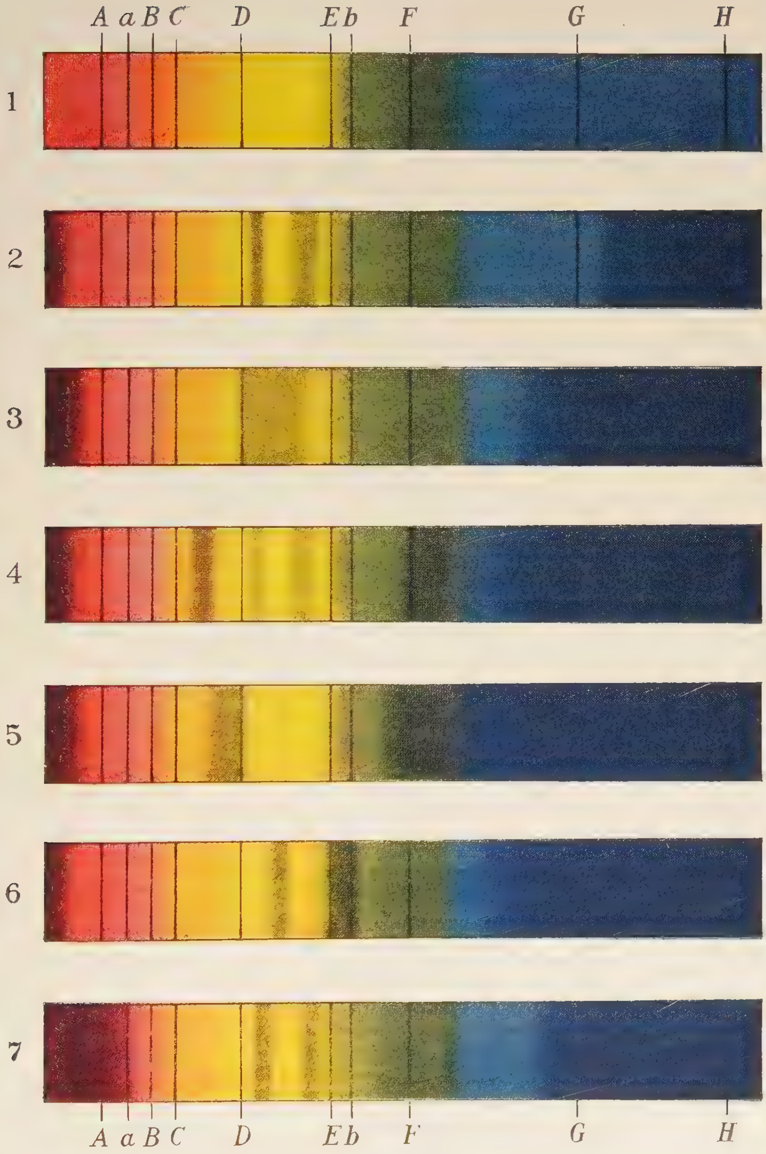
[1] An aqueous solution of ferrous sulphate to which tartaric acid has been added and then sufficient ammonia to render the mixture alkaline.

PLATE I

BLOOD SPECTRA



1. Solar spectrum.
2. Oxyhemoglobin.
3. Hemoglobin.
4. Methemoglobin in dilute solution.
5. Hematin in alkaline solution.
6. Hemochromogen, or reduced hematin.
7. Carbon-monoxide hemoglobin.

(From Hektoen and McNally, in Peterson, Haines, and Webster, "Legal Medicine and Toxicology.")

Methemoglobin.—This pigment is closely related to oxyhemoglobin, as it contains the same amount of oxygen and is isomeric with it, the oxygen being in more stable combination than is the case with oxyhemoglobin. A solution of methemoglobin shows spectroscopically a dark band in the red between C and D, lying a little nearer to C than to D. If properly diluted, two faint bands may be seen between D and E in a position similar to that of the oxyhemoglobin bands, and still a fourth band close to line F. As will be seen these lines of methemoglobin resemble those of hematin in acid solution, but are easily distinguished from the latter by the readiness with which the spectrum turns into that of hemoglobin on treatment with ammonium sulphide, while hematin, under the same conditions, yields the spectrum of hemochromogen, especially when the solution be alkalinized.

Hematin.—This pigment is found in old stains which have been subjected to varying atmospheric conditions for some time, or has been acted upon by chemical agents. It is found, also, under various pathological conditions in the body and in the urine, especially, in cases of poisoning with arsenic, but such conditions do not concern us here. Hematin is insoluble in water, dilute acids, alcohol, ether and chloroform, but dissolves readily in dilute alkali, acidified alcohol, or glacial acetic acid.

The spectrum of hematin differs with the acid or alkaline nature of the solvent. The acid hematin solutions absorb both ends of the spectrum, especially the violet, the absorption bands varying with the concentration and the acidity of the solution. The most prominent band is a sharp one between C and D, nearer C than D; a second broad but not clearly defined band between D and F, which may be resolved by varying the dilution into two bands, one dark and broad between β and F and the other faint and narrow near E; sometimes a fourth band may be seen as a faint narrow band just to the right of D. However, under usual conditions the band between C and D and the broad band between D and F are the only ones detected. Solutions of alkaline hematin show one absorption band between C and D, which reaches out to some extent between D and E, while the violet end of the spectrum will be almost absorbed.

Hemochromogen (Reduced Hematin).—As previously mentioned, if an alkaline solution of hematin be treated with such a reducing agent as ammonium sulphide or Stokes' reagent, hemochromogen is formed. The spectrum of this reduced hematin shows two characteristic absorption bands, one very sharp and dark between D and E and a second paler and broader band covering the E line. It is important to bear in mind that such an alkaline solution of hemochromogen absorbs oxygen fairly readily and is reconverted into hematin, so that such reduced solutions of hematin should be examined promptly.

Hematoporphyrin.—In very old stains, especially those that have been heated, great difficulty is experienced in dissolving the pigment by the ordinary agents, so that resort is had to treatment of such refractive stains with concentrated sulphuric acid, which converts the hematin into hematoporphyrin. This latter pigment does not exist as such in the blood stain, unless this has been subjected to treatment with strong acids or other agents which bring about the splitting off of iron from the hematin. The pigment, hematoporphyrin itself, is insoluble in water, but dissolves in alcohol, strong and weak alkalies and in acids.

The usual solution obtained for examination is that in concentrated sulphuric acid, which shows two absorption bands, one fainter and narrower between C and D and nearer D, the other darker, sharper and broader in the middle between D and E. If the solution be in dilute alkali, four absorption bands will be noted: A faint band between C and D, a second broader band surrounding D with the broadest part between D and E, a third between D and E nearly at E, and a fourth broad and dark between E and F.

Changes of Spectra.—It is important, in the study of the spectrum obtained from solutions prepared by extracting suspected stains with various solvents, to examine the effect of various agents upon the spectrum first observed. As we have seen, the bands of oxyhemoglobin may be changed into those of hemoglobin by treatment of the solution with a reducing agent; methemoglobin acts similarly, while hematin in alkaline solution gives hemochromogen under these conditions.

There are, however, a few substances of animal and vegetable origin which give spectra which may be confusing, although the lines are not exactly in the same position as those of the blood pigments. Hence, it may be necessary to differentiate these substances in order to forestall argument when on the witness-stand. The most important of these confusing red-colored substances are, according to Sorby, the following: the coloring matter of the petals of the red variety of Cineraria; cochineal in alum solution; lac-dye, alkanet, madder-red, and munjeet in alum solution. To differentiate these from blood solutions, proceed as follows: Add to the suspected solution, which has been preliminarily examined for its spectrum, some ammonia. In the case of blood solutions, the position of the bands is not altered although the intensity of the bands may be increased; while the bands produced by Cineraria, lac-dye, alkanet, madder-red and munjeet will be completely changed. In the case of cochineal, the position of the bands is not altered by ammonia, but, if a dilute boric acid solution be added, the cochineal bands immediately shift to the blue end of the spectrum, while those of blood remain unchanged. Further, with lac-dye, alkanet, madder-red and munjeet, the addition of a dilute solution of sulphite of sodium or potassium bleaches their solutions, while such treatment has no effect on solutions of blood. Similarly, a mixture of magenta and blood may show a spectrum, in which the absorption bands of blood are completely masked, but the addition of sulphite of sodium will completely remove the magneta coloring matter, leaving the spectrum of blood clear and definite. In spite of the possibility of such confusing substances being present, the transformation of the spectrum of blood pigment into other blood pigments, as for instance of oxyhemoglobin into hemoglobin by the action of reducing agents, is definite proof of the presence of blood, as the substances mentioned above, which give confusing spectra, are not changed by the action of reducing agents. We have, therefore, a double method of checking the presence of blood.

Microscopic Examination.—The microscopic examination of blood stains is directed toward the recognition of red blood cells and other cellular elements that may give some indication of the possible origin of the blood. The value of this type of examination depends upon the fact that the red cells of certain classes of animals differ from those of others, thus making it possible to decide as to the general class from which the blood is derived. The red cells of most mammals are circular, non-nucleated, biconcave, disk-shaped bodies, while in the camel tribe they are lanceolate-oval or elliptical in shape and non-nucleated and in the Mexican deer they appear circular, heart-shaped or crescentic. However, in birds, fishes, reptiles, and amphibians the red cells are oval in shape and have distinct nuclei, except in the lamprey and some fishes (cyclostomata) the cells are circular. It is clear that one will have little difficulty in differentiating the blood of a mammal from that of birds, reptiles, fishes, and amphibians, by careful observation of the presence of nuclei in the red cells. However, in distinguishing between the different kinds of mammalian blood, great difficulty arises.

It is undoubtedly true that the microscopic examination of blood stains in medicolegal cases cannot absolutely determine the mammal from which the blood came. The red blood corpuscles of different mammals differ more or less in size, in some cases this difference lying within such narrow limits that differentiation is practically impossible, especially under such conditions as usually obtain in medicolegal work; while in other cases the variation in size may be quite marked, so that one may definitely state that the blood is not that of human origin, for instance. In fresh blood, these differences in size of the corpuscles may be fairly accurately measured by means of reliable micrometer scales, but, when the blood has dried, great difficulty arises in making such measurements.

When the red blood cells are treated with water or with fluids that have a less osmotic pressure than has the blood serum, they become spherical in shape and lose their hemoglobin, the diameter of the cell becoming only about two-thirds its original diameter and the outlines of the cell becoming almost lost. If the cells are subjected to the action of a solution with a higher osmotic pressure than that of the serum, the cells become shrunken and the edges irregular forming what are called "crenated" cells. The cell becomes much smaller in size but does not lose its hemoglobin, so that it may be easily recognized. Changes in the red cells, present in the blood that forms the stain in question, Average Size of the Red Blood-cells

Mammals.	Gulliver.	Wormley.	Formad.	Richardson.	C. Schmidt, 1848.	French Medicolegal Society, 1873.	Masson, 1885.	Dragendorff.	Woodward.
Man	1–3200	1–3250	1–3200	1–3224	1–3330	1–3257	1–3256	1–3300	1–3092
Monkey	1–3412	1–3382	.....	1–3395					
Opossum	1–3557	1–3145							
Guinea-pig	1–3538	1–3223	1–3400	.....	.....	.....	1–3300	.....	1–3213
Kangaroo	1–3440	1–3410							
Musk-rat	1–3550	1–3282							
Dog	1–3532	1–3561	1–3580	1–3542	1–3630	1–3479	1–3577	1–3628	1–3246
Rabbit	1–3607	1–3653	1–3662	.....	1–3968	1–3681	1–3628	1–3968	
Rat	1–3754	1–3652	.....	.....	1–3968				
Mouse	1–3814	1–3743	.....	.....	1–4166				
Pig	1–4230	1–4268	1–4250	1–4230	1–4098	1–4233	1–4098	1–4098	
Ox	1–4267	1–4219	1–4200	1–4267	1–4385	1–4535	1–4233	1–4385	
Horse	1–4600	1–4243	1–4310	.....	1–4456	1–4535			
Cat	1–4404	1–4372	.....	.....	1–4535	1–3907	1–4456	1–4535	
Elk	1–3938	1–4384							
Buffalo	1–4586	1–4351							
Wolf (prairie)	1–3600	1–3422	1–3450						
Bear (black)	1–3693	1–3656							
Hyena	1–3735	1–3644							
Squirrel (red)	1–4000	1–4140							
Raccoon	1–3950	1–4084							
Elephant	1–2745	1–2738							
Leopard	1–4319	1–4390							
Hippopotamus	1–3429	1–3560							
Rhinoceros	1–3765	1–3649							
Whale	1–3099	.....	.....	1–3090					
Tapir	1–4000	1–4175							
Lion	1–4322	1–4143							
Ocelot	1–4220	1–3885							
Mule	.....	1–3760							
Ass	1–4000	1–3620							
Ground-squirrel	.....	1–4200							
Bat	1–4175	1–3966							
Sheep	1–5300	1–4912	1–5000	1–5300	1–5649	1–5080	.....	1–5649	

may be of either of these types depending upon conditions to which the cells are subjected, so that it is necessary, in selecting a portion of a dried stain for microscopic examination, to use the portion that has dried most quickly, that is as a rule near the periphery of the stain rather than from the center, as the shape and size of the cells from the outside will be more nearly normal.

The questions arising in medicolegal investigations are usually concerned with the possibility of the blood having come from a mammal or from a bird, reptile, fish or amphibian, and further, with the point as to whether the blood is that of a human or other mammal. As we have seen the first question is answerable from the presence or absence of nuclei in the cells. With the mammals, the size of the corpuscles must be considered before any approach to an answer may be given, The variation in size of the mammalian red cells runs from those of $1/6000$ inch to those $1/3000$ inch in diameter. The average diameter of the human red cell may be taken as about $1/3200$ inch, while that of the dog, the only domestic animal whose red cells might be confusing, is about $1/3550$ inch. The cells of the pig, horse, ox, cow, cat, sheep and goat all vary considerably from this, as may be seen from the accompanying table, so that if fairly accurate measurements can be made of cells found in stains, it may be possible to state that the cells found are consistent with a certain origin. The statement should never be made

AVERAGE SIZE OF THE RED BLOOD-CELLS (*Continued*)

MAMMALS.		Gulliver.	Wormley.	Formad.
Ibex		.....	1–6445	
Goat		1–6366	1–6189	1–6100
Sloth		1–2865		
Platypus (duck-billed)		1–3000		
Capybara		1–3190	1–3164	
Seal		1–3281		
Woodchuck		1–3484		
Musk-deer		1–12325		
Beaver		1–3325		
Porcupine		1–3369		
Llama	Long diameter	1–3361	1–3201	
	Short "	1–6229	1–6408	
Camel	Long "	1–3123	1–3331	
	Short "	1–5876	1–5280	
BIRDS.				
Chicken	Long diameter	1–2102	1–2080	
	Short "	1–3436	1–3483	
Turkey	Long "	1–2045	1–1894	
	Short "	1–3598	1–3444	
Duck	Long "	1–1937	1–1955	
	Short "	1–3424	1–3504	
Pigeon	Long "	1–1973	1–1892	
	Short "	1–3643	1–3804	
Goose	Long "	1–1836		
	Short "	1–3839		
Quail	Long "	1–2347		
	Short "	1–3470		
Dove	Long "	1–2005		
	Short "	1–3369		
Sparrow	Long "	1–2140		
	Short "	1–3500		
Owl	Long "	1–1763		
	Short "	1–4076		

REPTILES.		Gulliver.	Wormley.
Tortoise (land)	Long diameter	1–1252	1–1250
	Short "	1–2216	1–2200
Turtle (green)	Long "	1–1231	
	Short "	1–1882	
Boa constrictor	Long "	1–1440	1–1245
	Short "	1–2400	1–2538
Viper	Long "	1–1274	
	Short "	1–1800	
Lizard	Long "	1–1555	
	Short "	1–2743	
BATRACHIANS.			
Frog	Long diameter	1–1108	1–1089
	Short "	1–1821	1–1801
Toad	Long "	1–1043	
	Short "	1–2000	
Triton	Long "	1–848	
	Short "	1–1280	
Proteus	Long "	1–400	
	Short "	1–727	
Amphiuma tridactylum	Long "	1–363	1–358
	Short "	1–615	1–622
FISHES.			
Trout	Long diameter	1–1524	
	Short "	1–2460	
Perch	Long "	1–2099	
	Short "	1–2824	
Pike	Long "	1–2000	
	Short "	1–3555	
Eel	Long "	1–1745	
	Short "	1–2842	
Lamprey (Circular)		1–2134	
Lamprey (Diam. of Nucleus)		1–6400	

that cells are absolutely those of a definite mammal, as conditions under which the blood has been kept may so alter the size of the cells that measurements are uncertain. The examiner may state the average size of the cells found by him and, also, the average measurements of cells of different animals as reported by others, but he should not be lead, in spite of close agreement in size between his findings and those of others, to state any more than that the cells might be of such an origin. He may be able to say, from his examinations, that the blood in question could not have come from certain animals, but to state that it actually came from a definite animal is very unsafe.

Method of Examination.—We are not concerned here with the methods of microscopic examination of fresh blood, as drawn from the subject, but rather with the study of the cells from dried or pooled blood. A minute fragment of the dried material is scraped from the surface on which it is found by means of the point of a knife and the material placed upon a glass slide. If the stain be upon cloth a few fibers of the cloth may be teased out and placed on the slide. This stained material is then treated with a drop or two of such a fluid as will not alter the corpuscles but will soften and disintegrate the clot, and will have approximately the same specific gravity and osmotic pressure as has the blood serum. (For practical purposes the specific gravity of the serum may be taken as 1028). There are many such solutions recommended, but the following will usually serve the purpose: Physiologic salt solution (0.9 per cent sodium chloride solution); Virchow's fluid consisting of a 30 to 33 per cent. solution of caustic potash; Roussin's solution, a mixture of 3 parts of glycerol, 1 part of sulphuric acid, and water enough to yield a fluid with a specific gravity of 1028; saturated solution of borax in water; and finally distilled water, as recommended by Wormley, adding approximately the amount thought to be originally present in the blood under examination.

After selecting the solvent that is to be used, a cover glass is placed over the moist stain on the slide and sealed with cement to prevent evaporation. The preparation should be examined from time to time for red cells and, when these are found, they should be examined closely to determine whether they are normal cells or are swollen, disintegrated or crenated cells. Only those that appear normal should be measured. For the measurement a stage micrometer and an eye-piece micrometer are essential, the details of the use of which may be obtained from works on microscopy.

The Biologic or Precipitin Test.—This test is of special forensic value, inasmuch as by means of it the ultimate source of the blood stain may be determined, that is the species from which the blood came can, in most cases at least, be determined.[1] This test is based on the fact that when a rabbit is injected with foreign protein, its serum will form a precipitate when mixed with a solution of this foreign protein. This reaction is due to the production, in the serum of the rabbit, of so-called immune bodies, in this case of precipitins. The point of medicolegal importance in this connection is that these precipitins are specific, that is they precipitate, under certain conditions to be discussed, only the protein which is of the same species against which the rabbit has been immunized, and only this protein or ar least such proteins as are closely related to the type injected. It is possible, therefore, to immunize (inject with proteins) many rabbits, using one or more for each type of animal protein which may be in question in a particular case, so that one may be in a position to state that the blood is or is not derived from a certain species of animal. The test is now generally accepted in all courts as a specific one, so that it should never be neglected in the study of a blood stain.

Production of the Anti-serum or Precipitin Serum.—This is the serum of the animal immunized against the proteins of the blood, whose species we are attempting to determine. In medicolegal cases, while it is of chief importance to determine whether or not a given stain is of human origin, yet it may be also necessary to be able to say that it is not of bovine, ovine, canine or other origin. At the present time certain anti-sera, especially anti-human serum, can be purchased from the large biological supply houses and are found to be quite reliable. However, some courts raise the question as to whether you have prepared this serum yourself and, if you answer in the negative, may object to testimony based on its use. Such objections cannot be sustained, if you are able to show that properly made tests have been conducted to show the specificity of the serum and that you personally know what you are using. However, many experts prefer to prepare their own anti-sera or at least have it prepared under their supervision, in order to avoid any quibbling about the matter.

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[1] See "The Precipitin Test for Blood" by Hektoen and McNally in Legal Medicines and Toxicology by Peterson, Haines & Webster, 1923, **2**, 927.

As the animal to be injected, the rabbit is almost universally used, although some workers prefer the domestic male fowl. Young, healthy, unused animals should be selected, keeping them in good surroundings and feeding them plentifully. It is wise to inject several rabbits at the same time, so that one may be sure to obtain anti-serum of proper strength. Either whole blood, defibrinated or citrated, or serum may be injected. One may use either intravenous or intra-peritoneal injections of serum, but whole blood should not be injected intravenously.

Inject from 1 to 2 cc. of serum intravenously, repeat in about a week, and then after 6 or 8 days inject 4 or 5 cc. intraperitoneally. Or one may inject 5 or 6 cc. of blood or serum intraperitoneally four or five times at intervals of about a week. In about a week after the last injection, withdraw some of the blood from the animal by puncture of the ear, allow it to clot, and test the potency of the serum by tests to be described shortly. If the serum is found to be sufficiently potent and specific, the animal may be bled and a supply of the serum obtained for future tests. Place the serum in small bottles or tubes, each of 1 or 2 cc., add a few drops of chloroform as preservative and store in the ice box after proper labeling of the container. Occasionally the serum as prepared will be found to be opalescent. If it is, it is useless and should be discarded. The tendency to show this opalescence may usually be avoided by allowing the rabbit to fast for some 18 hours before it is bled.

Testing of Precipitin Serum.—Before a serum, obtained as outlined above, may be used in medicolegal cases, it must be shown to have a certain potency and, also, to have a strictly limited range of activity, that is to be specific in its action.

1. *Test for Potency.*—The object of this test is to find the highest dilution in salt solution (0.9 per cent.) of the serum or blood, homologous with that injected into the rabbit, with which the precipitin serum forms a precipitate in a few minutes at room temperature. For the purpose of this test, as also for use in the precipitin test proper, small, clean, clear, flat-bottomed glass tubes about 25 to 30 mm. long and 0.5 cm. in diameter are to be prefered. In each of a series of such tubes placed in a small rack, preferably a small wooden block with holes cut to fit the tubes, is placed a little of the antigen (homologous serum) dilution, in the first tube a dilution of 1:250, in the second 1:500, and so one through 1:1000, 1:1500, 1:2000, 1:2500, 1:3000, etc. By means of a small capillary pipet add at the bottom of each tube about 0.1 cc. of the antiserum, allowing

the serum to flow out below the antigen dilution so that the anti-serum does not mix with the antigen, but, rather, forms a distinct line of contact with it. The tubes are kept at room temperature and are examined at intervals of ½ minute for the appearance of a grayish-white precipitate at the zone of contact of the two fluids. If a precipitate forms almost immediately in the antigen dilution of 1:1000, the antiserum is regarded as sufficiently potent for forensic purposes. Such an antiserum will, undoubtedly, give a definite precipitate with much higher dilutions, if allowed to stand for 20 minutes, the time adopted as the limit for the test in forensic cases. The titer of the serum should be marked on the tube containing the antiserum for future reference.

If the test for potency is to be made with whole blood, the corpuscles are laked by means of water and an equal amount of 1.8 per cent. sodium chloride solution added, thus restoring the solution to a normal salt content. Later dilutions of this original solution are made, of course, with physiological salt solution.

In reading ones results of this potency test, as also in the test itself, the small tubes are held, as advised by Hektoen, near a black, flat object, such as a book cover or ruler, directly in the path of the light, when the precipitate will be distinctly seen, first composed of fine particles and sharply defined and later possibly becoming flocculent and sinking to the bottom.

2. *Tests for Specificity.*—This phase of the subject is so ably presented by Hektoen[1] that I quote him directly: "On account of the relationships of species, almost every strong precipitin serum may form precipitates with proteins, at least in low dilutions, of species related to that species, the blood proteins of which were used for the production of the serum. Indeed, any strong antimammalian serum may react in low dilutions—1:10 or so—of mammalian serums or blood generally. This is the mammalian reaction of Nuttall. In the case of kindred species, the precipitin affinities often are more marked; for instance, an antigoat serum may react in high dilutions of sheep and beef as well as of goat serum or blood. Further examples of closely related groups are the horse, ass, and mule; the dog, wolf, and fox; the domestic fowl, turkey, goose, duck, and pigeon; the hare and the rabbit, each with more or less pronounced common precipitin reactions. Man and monkey, from the highest down, constitute another group with special precipitin inter-reactions between the members. How it nevertheless may be possible by the precipitin test to identify the blood of the individual species is discussed later. As each antiserum may vary in the number and strength of its group and other precipitins, and as it must be known to be free from non-specific reactions before it is used, it is necessary, besides fixing its potency, to determine the exact range of its action. The test for specificity is carried out in the same manner in general as the test for

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[1] Loc. cit. p. 931.

potency; that is to say, tubes are prepared in the same way with dilutions of as many other serums or bloods beside that used in the production of the serum as seem necessary to afford a thorough test, certainly not less than two, the antiserum added as before, and the results noted. At the same time the antiserum is tested with salt solution only to determine whether any precipitate then forms.

"A usable antiserum must be perfectly clear; it must have a certain minimum specific precipitin strength, and it must not give any misleading non-specific reactions. To illustrate: If an antihuman serum is perfectly clear; if it forms a precipitate practically at once in a 1:1000 or higher dilution of human blood or serum; and if with that of any other species, then in very low dilutions only, say from 1:10 to 1:100, and much more slowly, save possibly in the case of the monkey (group reaction); and if it does not form any precipitate with salt solution, then it may be used for tests for human blood for forensic purposes."

Preparation of Material for Precipitin Test.—The articles submitted for examination of suspected spots and stains comprise almost every sort of conceivable object, so that the examiner may be required to use different methods of extraction. The best solvent for use in this test is, of course, 0.9 per cent. salt solution, but occasionally it is wise to use distilled water as the preliminary solvent in order to lake the blood cells that may be present. If this latter procedure be used, the aqueous extract should be diluted with an equal amount of a 1.8 per cent. salt solution, thus bringing the final extract to the normal concentration. If the stain be dried upon solid material, such as glass, knife blade, stone, wood, etc., it may usually be scraped off with the point of a clean knife. This material is powdered and mixed with a small quantity of the physiological salt solution. If the stain be upon pieces of cloth, paper, straw, cork, rubber, leather, lime, mortar, earth, etc., portions of the material containing the stain should be placed in a small test-tube and a small amount of water or salt solution added, portions of the unstained material being treated in the same manner to serve as controls. It is occasionally found that these methods do not yield satisfactory results, as the age of the stain, its length of exposure to the elements, and possible heating or chemical treatment may affect the solubility. Under such conditions, one may extract the stained material with a 1 per cent. solution of potassium cyanide, neutralizing the alkalinity after extraction with a weak solution of tartaric acid as advised by Sutherland, although this method does not always prove reliable.

The length of time necessary to extract with salt solution will depend, of course, on the age and the condition of the stain. These points have been previously discussed. The strength of the extract required in the precipitin test is 1:1000, so that with fresh blood stains the extract may require dilution with normal salt solution. However, with the more refractory stains this is not usual. In order to determine approximately as to the concentration of the extract, one may shake the tube containing the extract and observe whether or not a layer of foam forms on the surface of the liquid, or may blow into the fluid through a capillary tube when the bubbles formed will tend to persist, and, further, on heating a little of the extract and adding a drop of 25 per cent. nitric acid only a slight opalescence should obtain. There will be practically no red color in a solution of such a dilution as 1:1000. The above tests indicate that protein has passed into solution in the solvent and that the amount of it is roughly about 1:1000. If the nitric acid reaction should be more intense or if the color should be distinctly red, the extract should be diluted with salt solution. If the above tests should show that little extraction of protein has occurred, the tube should be placed in the ice box and the extraction allowed to continue over night. With fresh stains, extraction is rapid, while with older stains the period required may vary from 1 hour to 24 hours.

The final fluid to be used in the precipitin test must be clear; if it is turbid it may be cleared by centrifugation or filtration through hardened filter paper or, if necessary, through a small Berkefeld filter. The reaction must be practically neutral to litmus, neutralization, if necessary, being effected by a 0.1 per cent. solution of sodium hydroxide or of hydrochloric acid as the case may require. Further, this fluid should show distinct foam-formation on shaking and should give only a slight opalescence on the addition of 25 per cent. nitric acid to the warm solution, as evidence of proper concentration.

Technic of the Precipitin Test.—The reactions are carried out in the small tubes previously spoken of, which must be clean and clear, and preferably sterile, although if the reactions are promptly carried out bacterial action will have little chance to affect the results. The tubes should be flat-bottomed and 25 to 30 mm. long and 0.5 cm. in diameter, while the capillary pipets employed are made by drawing out glass tubing in the usual manner. A good supply of both tubes and pipets should be on hand for the work.

In setting up the tubes for the test, at least 10 should be used, numbering each or placing each in a numbered place in the block for the purpose. Specimens of blood of various types should be on hand to be used as controls, as many different kinds being employed as can conveniently be obtained. In any case, if there is any question of the presence of a certain type of blood being present, this should be used as a control, to be able to say that the anti-human serum did not act with such blood, and, further, a second test should be run with the extract of the stain, using an anti-serum for the blood in question and running through the test just as performed when anti-human serum was employed.

The tubes for the test are set up as follows, each tube containing 0.5 cc. of the solution named: Tubes 1 and 2, extract of the stain in question; tube 3, extract from a non-stained portion of the material from which the suspected stain was taken; tube 4, normal salt solution; tube 5, known human blood extract 1:1000; tubes 6 to 10 inclusive, 1:1000 extract of blood other than human. To each of the tubes with exception of tube 2 are added with a capillary pipet 0.1 cc. of antihuman rabbit serum and to tube 2 is added 0.1 cc. of normal rabbit serum. The antiserum should be added in such a way that a distinct line of contact is formed between the extracts and the serum, this being best accomplished by introducing the pipet to the bottom of the small tube and allowing the serum to flow out below the extract.

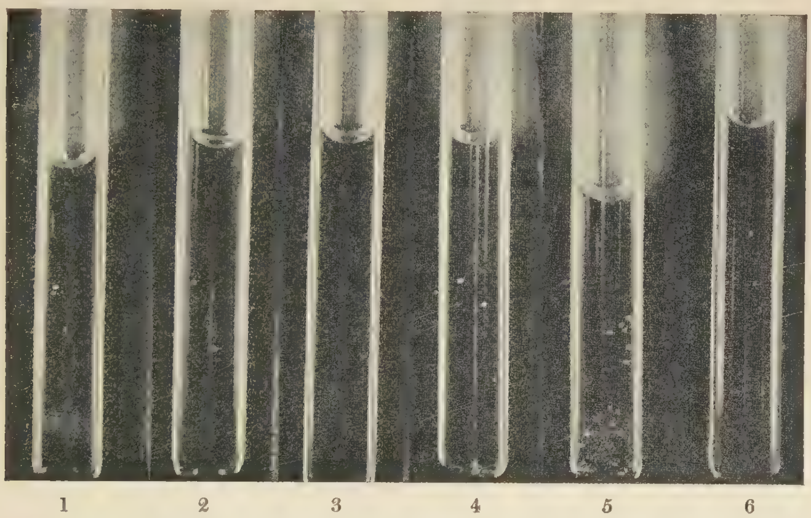

Fig. 22.—Precipitin test for human blood: Tube 1, Extract of blood on shirt of estimated dilution 1:1000 + antihuman rabbit serum; Tube 2, extract of blood on shirt of estimated dilution 1:1000 + normal rabbit serum; Tube 3, extract of bloodless part of shirt + antihuman rabbit serum; Tube 4, salt solution + antihuman rabbit serum; Tube 5, dilution of human blood 1:1000 + antihuman rabbit serum; Tube 6, dilution of sheep blood 1:1000 + antihuman rabbit serum. The precipitates in Tubes 1 and 5 formed almost at once; photograph was taken from five to eight minutes after introduction of the antiserum. (From Hektoen and McNally, in Peterson, Haines and Webster, "Legal Medicine and Toxicology.")

If a typical white precipitate appears at the zone of contact of the two liquids within a minute or two in tubes 1 and 5, while no precipitate forms in any of the other tubes after standing for twenty minutes at room temperature, then one is justified in stating that human protein is present in the stain. After obtaining a positive reaction with an extract of approximately 1:1000 dilution, one may dilute his extract in an increasing manner and determine the highest approximate dilution that will react with antihuman serum in twenty minutes at room temperature, thus verifying the specificity of his reaction and excluding the possibility of other proteins being accountable for the positive reaction.

Medicolegal Value of the Precipitin Test.—It must be remembered that this test is directed toward the detection of protein material, which is of the same origin as that injected into the rabbit in order to produce antiserum. It is in no way a test for blood, except in so far as blood contains protein material. One is never able to say from this test alone that a specific *blood* is present, as the presence of blood must be shown by the other tests outlined. The immune serum reacts promptly with the protein elements of exudates, sputum, pus, urine, feces, milk, nasal and bronchial secretions, vaginal, lochial and seminal fluids, etc., so that a positive precipitin test means merely that an homologous protein is present.

Although this test is extremely delicate, yet it may happen that a stain, definitely identified as a blood stain by other tests, may not react typically to the precipitin test, owing to the very small amount of protein matter in the extract. The power of the blood to react with the antiserum may be reduced or completely destroyed by alcohol, formaldehyde, cresol, corrosive sublimate, acids and alkalies, by peptic digestion, by decomposition, and by heat. Tannic acid, derived from stains upon leather or oak wood, may prevent the reaction in some cases, although this is not always the case, while iron rust retards but does not prevent the reaction. As far as the influence of time upon this reaction is concerned, it is to be said that blood stains over 50 years old have been successfully identified. The whole point in this connection is whether any trace of soluble protein remains; if it does the test will be successful.

If the conditions of the test are properly maintained as outlined above, non-specific reactions do not occur. It is true that confusing reactions may arise in the differentiation of group reactions, such for instance as the horse, ass and mule; goat, sheep and ox; dog and fox; hare and rabbit; chicken and pigeon; man and monkey. However, if proper attention be paid to the dilution in which the given antiserum reacts, it will be found that homologous blood reacts in the higher dilutions, while the related bloods show precipitation only in much lower dilutions. While it is most important to establish the presence or absence of human blood in a given stain, yet in some cases it may be necessary to find out whether or not there may be other protein than human in the stain. In such cases the test is run, exactly as outlined above, using the antiserum for the blood in question, instead of the antihuman serum discussed above.

In some cases the point is raised by the defense that the stain on the clothing or other articles in question is not due to human blood, but to animal blood falling on spots stained with albuminous material of human origin but not derived from human blood. Such composite stains would give, of course, the precipitin reaction for human protein, would show reactions for blood by chemical and spectroscopic tests, and might show corpuscles, whose size might be very confusing, as for instance if the blood was of canine origin. Under these conditions the worker would fall into difficulty if he stated that the stain was definitely due to human blood. If the corpuscles admit of exact measurement, it might be possible to show that they were of canine rather than of human origin, although this would be a close proposition, but a precipitin test, using anticanine serum would show whether or not there was dog protein present. If we could go no further, the situation might possibly be clouded by such a complication, as one might not be in a position to state definitely the composition of the stain. In such cases it is probable that the specific erythroprecipitin (antihemoglobin) serums will solve the question definitely. As Hektoen and Schulhof[1] remark: "The precipitin test for hemoglobin is fully as specific and as sensitive as the precipitin test for serum, if not more so. The possible overlapping of the reaction in related species merits consideration and further study, and naturally careful control tests must be made in all cases. The advantage of the hemoglobin test should be that it is a direct test for blood only. The serum precipitin test is a test for species protein in general, and whether blood is present is determined by other and nonspecific tests. Now it is possible that a blood spot giving a precipitin reaction for human protein and, therefore, apparently human blood might be made or claimed to be made by animal blood falling on a place previously stained by human protein in sputum, albuminous urine or any kind of bloodless exudate. In problems of this kind, the precipitin test for hemoglobin may be of decisive value." For the details of preparation of these hemoglobin precipitin serums, the reader should consult the articles cited above. Recently Hektoen and Schulhof[2] have shown that the antigenic group of hemoglobin forms a part of the molecule which may be split off by acids. They believe that it is probable that this antigen is globin, but they admit that there is a possibility of a third group which may be responsible for the reaction.

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[1] Jour. Inf. Dis., 1922, **31,** 32; Ibid., 1923, **33,** 224. See, also, Fujiwara, Deutsch. Ztschr. f. d. ges. ger. Med., 1928, **11,** 253.

[2] Ibid., 1927, **41,** 476.

CHAPTER X

IMPOTENCE AND STERILITY

In connection with these subjects there often arise many points which have to do with questions of legitimacy or paternity, with marriage and divorce, and with alleged rape and other sexual assaults. As Chaddock remarks[1]: "The importance of such possibilities in their relations to marriage and the family calls for examination of the various conditions that constitute or occasion lack of sexual power or absence of ability to fecundate on the part of the male, and of those conditions affecting the female which render fecundation impossible."

The terms impotence and sterility are often confounded, both being used by some writers to express lack of procreative power, the former in the male and the latter in the female. Thus, Reese[2] states that "Impotence, or the want of procreative power in the male, may be functional or organic. The term sterility, when applied to the female, is usually understood to mean an inability to conceive." Both of these terms apply equally to either sex, although it is true that some authors do limit impotence to men and sterility to women, but this is again quite erroneous. Impotence, as we shall use it, means incapacity for or impossibility of accomplishing the sexual act; while sterility refers to inability to procreate the species. As we shall see, it is perfectly possible for a man to be impotent and not sterile, and, on the other hand, for him to be sterile and not impotent. In the case of a woman, impotency rarely exists as a non-remedial condition, with the possible exception of more or less complete obliteration of the vagina, while sterility is quite common with women. It is unfortunate, however, that woman has been branded as the one most frequently at fault in the case of barren marriages. Thus, Rosse[3] states: "When a marriage is sterile it is, nine times out of ten, the woman who is to blame." That this point is debatable at least is shown by the statements of Talmey[4] who asserts: "Half the sterile marriages are due to azoöspermia of the male as the result of gonorrhea, and at least 90 per cent. of the other half, due to the female inability to procreate, is also caused by the infection the wife has received from her husband."

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[1] "Impotence and Sterility", in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **I**, 1023.

[2] *Medical Jurisprudence and Toxicology*, 8th ed. 1911, 261.

[3] "Impotence and Sterility", in *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 1907, **2**, 628.

[4] Medical Record, 1921, **100**, 631.

IMPOTENCE

Impotence may arise from physical or psychic causes, from congenital or acquired malformations or defects of the genital organs, or may be associated with the age of the individual. In the legal consideration of impotence, while any of the causes to be mentioned may be alleged to account for the condition, yet the law will not recognize as a basis for annulment of marriage or for divorce any one of such causes as may be remediable either by medical or surgical means. The court will insist upon knowing whether, in the opinion of the examining physician, the existing cause of the impotence or sterility is remediable or irremediable. If the condition is impossible of correction, a decree will usually follow. In this connection it should be said that refusal, on the part of the party accused of impotence to submit to treatment for removal of the obstacle to coitus, will warrant an annulment of marriage.

While it is true that the part of the male in the sexual act consists in immission of the penis and emission of semen, yet it is not necessary that the seminal fluid be potent. In other words the law does not take into account the question of sterility in the male in its consideration of impotence. The law regards coitus of man and wife as one of the material considerations of the marriage contract. If one of the parties cannot perform his or her part of that consideration, the courts will logically decree that the objects of the contract cannot be carried out and release the parties from their contract.

Impotence from Age.—The age of puberty in an ordinary healthy male varies from 14 to 17 years, although its appearance may be earlier or later, depending upon climate, constitution of the individual, and the surroundings under which he develops. While the sexual function in the male depends entirely on the development of the testicles, that is a male does not become capable of procreation until the appearance of spermatozoa in the sexual secretion, yet the power of erection of the penis and, therefore, the capability of coitus may be present at a much earlier age than that of puberty. Tidy[1] cites a case of a boy 4½ years of age attempting intercourse with his sister aged 2 years; while Koplik[2] gives a case in which two boys, aged five and nine, acquired gonorrhea by intercourse with a girl of seven. Cases are on record in which a boy of ten years has been convicted of rape, while boys of 13 and of 14 have been fathers of children. It is evident, therefore, that factors other than mere age must be taken into consideration in the study of the possibility of intercourse, and the courts usually rule that physical capacity must be determined by other evidence in any special case. While extreme youth must be regarded as a usual cause of impotence, yet the exact age at which a male becomes capable of coitus must be determined for each individual.

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[1] *Legal Medicine*, 1884, **3**, 7.

[2] Jour. Cut. and Gen.-Urinary Dis., 1893, p. 275.

In advanced age the power of erection and capability of coitus may disappear, but there is no specific age when this may occur and, in many individuals, it never does occur. Old age, *per se*, cannot be regarded as necessarily associated with sterility, much less with sexual incapacity. Impotence from advanced age does not, however, form an impediment to marriage, as the legal presumption is that the generative function is persistent. This point was established in the Banbury Peerage Case[1] in which it was stated by Romilly that "The law places no limits on the powers and faculties of man in respect of procreation." Rüttel[2] mentions the case of a man who married at the age of 92 and had two children by his wife, and there are many such cases between the ages of 70 and 80. Although the procreative power may be lost at various ages, yet it is equally true that all desire for sexual intercourse does not cease in these persons. On the other hand, as long as spermatozoa exist in the seminal fluid, procreation is possible, although such individuals may be incapable of intercourse on account of bodily infirmity. The point involved here is not that of the age of the individual but, rather, whether or not the seminal fluid contains spermatozoa. Taylor states that "Facts tend to render it highly probable that a fecundating power may be retained by the male up to the age of 100" and Casper[3] cites a case in which spermatozoa were actually found in an invalid 96 years old. As pointed out by Tidy, however, there is evidence to show that the seminal secretion of the same individual may change from time to time, so that an absence of spermatozoa is by itself to be regarded as proof neither of previous sterility, nor of the impossibility of subsequent fruitful intercourse, unless several examinations have been repeatedly negative. Hence, it is evident that, in cases of alleged impotence or of sterility of the male due to premature or advanced age, the point must be proven by a study of the various factors present in the individual case.

The age of the female has little influence on the question of impotence, except that very young girls are not capable of coitus owing to the small size of the parts involved. However, there are numerous cases reported of rape or assault on young girls by young boys or men, so that here the most important point to consider is whether there is sufficient development of the external genitalia to permit of mere penetration of the vulva. As the woman's part in sexual congress is largely passive, impotence is much less usual or open to disturbance than in the male. Certainly age does not influence this to any extent, as sexual desire is present at least from the age of puberty and intercourse, in the case of a married woman, continues just so long as there is functional capacity on the part of her partner and there is no bodily infirmity on her part which renders the act unpleasant to her or impossible of accomplishment.

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[1] House of Lords, 1806, 2 Peerage Claims, 48.

[2] Cited by Taylor, Medical Jurisprudence, 12th Amer. Ed., 1897, p. 655.

[3] *Forensic Medicine,* New Sydenham Society Edition, 1864, **3**, 291.

It is undoubtedly true that many women are never excited sexually and rarely experience a sexual orgasm, even though accustomed to frequent intercourse, and such women may gradually acquire such a mental aversion to the act as to become psychically impotent. On the other hand, there are women of such excessive ardor, that their demands upon their male partner sooner or later may lead to sexual incapacity or, at least, to temporary absence of spermatozoa from the seminal fluid.

Impotence from General Diseases.—There are undoubtedly a number of cases of impotence in men with well-formed and healthy generative organs, but who have no desire for sexual intercourse or are incapable of accomplishing it, owing to temporary disease. It is probably a general rule that diseases, which affect neither the brain nor spinal cord and which are not associated with great bodily weakness, do not cause impotency; while diseases which are associated with or followed by marked debility or with cerebral disease suspend or even destroy sexual power. As the sexual function is intimately associated with physical vigor and nervous energy, any marked disturbance of the latter influences the former. Among the diseases, which may produce at least a temporary impotence, we find renal disease, especially if edema involves the sexual organs, prostatic affections, disease or injury of the nervous centers, locomotor ataxia and dementia paralytica. Blows on the head or spine may produce impotence. Chronic alcoholism, morphinism, and excessive use of tobacco may all diminish or destroy virility.

Impotence from Local Malformations or Disease.—As the sexual act is dependent upon immision of the penis, anything which interferes with the proper immission will render the person impotent. Defects of development of the penis vary in degree from slight abnormalities of form to very small size or even complete absence of the organ. If the defects in form do not interfere with erection, they do not as a rule prevent intercourse. If the penis be extremely small, coitus may be difficult, but probably is not impossible. It is to be remembered here that, although the coitus under these conditions may be unsatisfactory to the wife, yet if the organ is sufficiently large to penetrate the vulva, emission of semen may occur and fecundation becomes possible, even though the hymen be unruptured. Such an individual is not, strictly speaking impotent, although charges may be made to that effect. Possibly, under the rulings in the Drane *v.* Aveling case, which we shall mention shortly, the wife could obtain an annulment on the ground of unsatisfactory coitus in such a case. In rare instances the penis is congenitally absent, while the other organs are normally developed, or the penis may have been removed on account of disease or injury. Such cases are, of course, impotent, although the individual may still have sexual desires.

There are, on the other hand, instances of excessive development of the penis, which may tend to prevent sexual intercourse or at least make it so uncomfortable for the woman that refusal to copulate is a common occurrence. Such individuals are not impotent, although attempts to procure divorce not infrequently are made on the ground of sexual incompatibility or of cruelty. Further, there are cases of double penis, which may cause difficulty in intercourse, but coitus is, nevertheless, possible.

As regards such abnormalities of development as are classed under the heading of hermaphrodism, we shall simply say that the real sex of the individual is determinable more on the basis of the internal organs of generation than on the external ones, and on the presence of menstruation on the one hand, or of seminal emissions on the other. It is probably true that most hermaphrodites are sterile and many of them impotent, although the law allows them to marry, providing the sex can be properly determined, so that their partner will be one of the opposite sex.

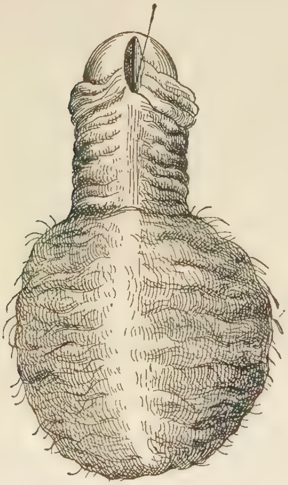

FIG. 23.—Slight hypospadias. (Hofmann.)

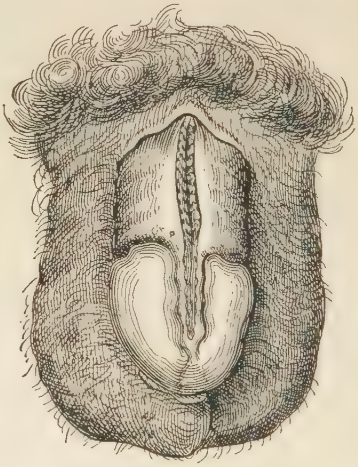

FIG. 24.—Epispadias. (Hofmann.)

There are two anomalies of development, hypospadias and epispadias, which may or may not interfere with copulation, but as a rule they do not render the subject impotent. Hypospadias is characterized by the opening of the urethra on the under side of the penis instead of at its normal apical position at the glans penis. Most of these cases show the opening just below the apex of the glans, and are, therefore, not to be regarded as rendering the individual impotent or sterile. However, when the opening of the urethra is low down between the glans and the root of the penis, or even in the raphe itself, procreation may be impossible owing to the fact that the semen is not discharged into the vagina during coitus, yet capability of intercourse is present. If the abnormality is associated with marked deformity of the penis, intromission would not be possible and impotency would obtain. In the case of epispadias, the opening of the urethra is on the upper side of the glans, on the dorsum of the penis, or close to its attachment. This condition is usually associated with a more or less rudimentary form of the penis, so that copulation may be impossible. Each case must, however, be studied by itself to determine the possibility of coitus, as no generalizations are pertinent.

Local results of disease, such as phimosis, paraphimosis, and large condylomata, may effect the ability to copulate, but these conditions are only temporary and are rarely to be considered in forensic cases. However, tumors of the genital organs or about these organs, large scrotal hernias, hydrocele, etc., may prevent coitus and temporarily render the individual impotent.

Impotence from psychic causes may be the result of masturbation or over-indulgence in sexual intercourse, the individual having a fear of impotence, or, having actually exhausted his store of nervous energy, losing his sexual desire and becoming incapable of coitus.

There are many conditions *in the female* that may render her temporarily impotent. Thus marked deformities of the pelvis, adhesion of the labia, imperforate hymen, marked prolapse of the uterus, and atresia of the vagina, may prevent intercourse, but these conditions are all remedial by surgical intervention. Probably the only cause of complete and permanent impotence in the female is absence of the vagina. Cases of obstinate vaginismus prevent coitus, owing to the pain occasioned the woman or to the contraction of the constrictor muscle of the vagina preventing entrance of the penis, but this condition is remedial. An interesting case in connection with partial contraction of the vagina is that of Drane *v.* Aveling[1] in which the facts were as follows: The external sexual organs, and the development necessary to the creation of sexual desire and gratification were perfect; but the vagina was contracted in depth, admitting of penetration to perhaps less than half the usual extent, and becoming impervious at that depth, where it formed a cul-de-sac, with no communication to any of the internal organs. There was an entire absence of uterus. The only impediment, therefore, so far as copulation was concerned, was in the restricted depth to which penetration could extend, and from the imperfect intercourse permissable. Upon these facts, and solely because no complete copulation could take place, the marriage was annuled. In announcing the decision, the judge, Lushington, said: "Mere incapability of conception is not a sufficient ground whereon to found a decree of nullity. The only question is, whether a female is or is not capable of sexual intercourse; or, if at present incapacitated, whether that incapacity admits of removal. A power of sexual intercourse is necessary to constitute legally the marriage-bond, and this intercourse must be ordinary and complete, not partial and imperfect; yet it would not be proper to say that every degree of imperfection would deprive it of its natural character. If it be so imperfect as to be scarcely natural, it is, legally speaking, no intercourse at all."

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[1] Robertson, 279. Cited by Tidy, *Legal Medicine*, 1884, **3**, 64.

STERILITY

In the Male.—As the power of procreation depends upon the presence of spermatozoa in the seminal fluid, sterility in the male is dependent upon some anomaly of the testicles or seminal passages or to pathological conditions which prevent the passage of the spermatozoa into the ejaculated fluid. Absence of the testicles would cause complete sterility. However, the fact that the testicles have not descended into the scrotum does not, of itself, indicate sterility, as many cryptorchids are prolific as shown by the literature on the subject. If, along with the non-descent of the testicles, there is no development of the other organs and a lack of the characteristics of virility, the subject may be regarded as sterile, although each case must be studied on its own merits. Castration or accidental loss of the testicles is not necessarily accompanied by impotence, although sterility is present. Loss of one testicle does not interfere with the procreative power if the remaining one be normal.

Although the sexual desire diminishes as age advances and the power of procreation diminishes as a rule, yet as previously stated there is no age at which the male may be said to be incapable of procreation as the seminal fluid may contain spermatozoa up to a very advanced age (96 in one case reported).

The most frequent cause of sterility in the male is bilateral inflammation of the spermatic ducts and the epididymis of gonorrheal origin. In such cases the canals are obliterated so that no spermatozoa are found in the ejaculation. Congenital malformations interfering with the escape of the spermatic fluid, or urethral stricture, usually of gonorrheal origin, likewise prevent spermatozoa finding their way into the fluid discharged. In these inflammatory cases, atrophy of the testicles may result, so that even if the ducts are not completely occluded, gradual sterility may ensue. Further, marked disease of the testicles or of the penis, such as syphilis, cancer, and tuberculosis, may be a cause of both impotency and sterility. In most cases of advanced age, there is a gradual atrophy of the testes, so that spermatozoa may disappear long before any sign of senile impotence appears.[1]

In the Female.—Probably the female is more frequently sterile than is the male, although, as stated by Talmey, her sterility is largely due to gonorrheal infection transmitted to her by the male. Procreative power in the female begins with the occurrence of menstruation, which is usually established between the ages of 14 and 16, but it may occur earlier and, in some rare cases, may not appear for years after. It is important to remember that sexual maturity may occur before menstruation appears, as this point may be raised in cases of alleged pregnancy. A woman may conceive before menstruation has commenced, during the time of its occurrence, or even after it has ceased. Capability of conception usually ceases between the ages of 45 and 50, menstruation stopping at about these periods. However, the stoppage of menstruation does not necessarily coincide with the power to conceive, as there are cases in which women have given birth to children some years after the menopause. Taylor states that "A woman over fifty-five years of age may be considered as past the age of child-bearing." Yet, as we shall see in the discussion of Pregnancy, children have been born to women many years after the age of 55.

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[1] See Kretschmer, "The Medicolegal Relations of Venereal and Genito-Urinary Disorders," in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, I, 1087.

Congenital absence or defect of the ovaries is found and is associated with defects in other genital organs. Removal of the ovaries for pathological reasons renders the woman sterile, unless there be a small portion of one ovary left intact. Inflammatory processes of the ovaries or tubes, usually of gonorrheal origin, ordinarily result in sterility. Abnormal position of the uterus, large, benign or malignant growths of the uterus, and inflammatory processes in the uterus, may cause sterility, although not in all cases. Narrowness of the vagina, and especially when associated with other genital defects, is a cause of sterility, although this may not be invariable. Absence of a vagina is, of course, a complete prevention of conception. Further, a pathological condition of the secretions of the vagina may render the spermatozoa innocuous, so that examinations should be made especially for marked acidity of these secretions. "Complete study of a sterility problem often reveals two or more conditions, each of which alone would be sufficient to prevent conception."[1]

MEDICOLEGAL RELATIONS

The principal medicolegal relations of impotence and sterility have reference to annulment of marriage and divorce, to paternity and affiliation, to legitimacy, and to alleged sexual assaults. At this time we shall discuss only the phases of the subject which have to do with marriage and divorce, leaving for later consideration the applications to the other points.

"Marriage is a contract having its origin in the law of nature antecedent to all civil institutions, but adopted by political society and charged thereby with various civil obligations. It is founded on mutual consent, which is the essence of all contracts, and is entered into by two persons of different sexes, with the view of their mutual comfort and support, and for the procreation of children." The contract of marriage differs from other contracts in that the parties thereto cannot release one another from the observance of the contract at will, nor can they annul the contract if certain points of the contract cannot be fulfilled. Such a procedure can be brought about only through a decree of court. This contract presupposes the capability of sexual intercourse on the part of both parties, so that any cause whatever, on the part of either party, which prevents coitus, would lead to possible severance of the contract.

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[1] See Meaker, Jour. Amer. Med. Assoc., 1928, **90,** 111; Ibid., 1929, **92,** 1493.

Up to relatively recent times the law has concerned itself only with such questions as might arise after marriage had occurred, but in more recent years efforts have been made in many states to regulate marriage by the adoption of the so-called "eugenic" laws, with which our present discussion has nothing to do. The laws of the various states differ widely as to what shall constitute grounds for annulment, divorce, or separation, and the distinction between a void and a voidable marriage is far from uniform. In general it may be said that all unmarried persons are legally capable of marriage provided they are of sufficient age and possess enough mental capacity at the time of marriage to give the necessary consent to the contract involved, although the recent eugenic qualifications and other health provisos may alter the status of some individuals in certain states.

If a marriage, which has been entered into in good faith by two parties of opposite sex, is not consummated by sexual intercourse owing to the discovery of such an irremediable physical defect as makes coitus impossible, the legal decree of separation of these parties is known as *annulment of marriage*, while if the marriage has been consummated the degree of a competent court is that of divorce, or in some jurisdictions, one of separation. This physical incapacity must date from the beginning of marriage (*ab initio*) and should not be something that has occurred after marriage. It is important to recognize here that the courts interpret this physical condition to be relative to the capability of performing proper sexual congress rather than to inability to procreate. In other words it is not *impotentia seminalis* but rather *impotentia copulandi* that constitutes legal impotence. Sterility in itself does not constitute a cause for annulment of the marriage. The physical inability to perform coitus must be one that is not remediable, if the suit for annulment is to be maintained.

Legally speaking, the impediment to coitus may consist simply in the deliberate refusal of either party to enter into coitus, due to the so-called frigidity of constitution or to purely psychic impotence, or may be the result of such a sensitive condition of the genital organs that it is not possible for coitus to occur without extreme pain or without administration of drugs to overcome the condition. The law assumes that the power to consummate the marriage is present, when the marriage bond is entered into, so that such refusal to permit intercourse may be regarded as possible *prima facie* evidence of impotence, although wilful refusal on the part of a wife to perform the sexual act is not in itself justification for legal interference unless persisted in so long as to give a presumption of impotence. Such refusal has been held to be no proof of impotence.[1] In cases of alleged impotence, the refusal of the accused party to accept reasonable and proper treatment is taken as a conclusive presumption that impotence exists.

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[1] See Merrill *v.* Merrill, 126 Mass. 228.

It is important to recognize in this connection that the cause of the physical incapacity on the part of the married couple may be due to purely psychic causes, which in some cases may be remedied, while in others they cannot. The parties may have made *bona fide* attempts to consummate the marriage and may have failed, in spite of the fact that there are no physical obstacles present. This constitutes the so-called sexual incompatibility. The same parties, who are incapable of sexual congress with one another, are oftentimes very prolific when married to others.

The impotence must have been unknown to the plaintiff in the case at the time of marriage. It is important here that the plaintiff does not waive his right to obtain relief from the situation by too long a delay, although some time must be allowed to establish a presumption of the existence of an actual impotence. Becker[1] believes that the marriage might be annuled at the suit of the impotent person himself provided he was honestly ignorant of his condition.

In determining the question of the existence of impotence and possible sterility, the physician is called upon to make an examination of the parties concerned. It is probably better practice for the same physician not to examine both parties. The examiner should be guarded in giving his opinion, when asked the direct question as to whether the man possesses the power of copulation, and should state that his examination reveals nothing that would justify an opinion that the individual was incapable of coitus. As Casper states: "The possession of virile and procreative power, neither requires to be, nor can be, proved to exist by any physician." This function is supposed to be present and the local conditions must determine the possibility of intercourse. Due consideration must be given to the mutual relationships of the sexual organs of the two persons, as what might be impotency with one individual might possibly not apply to another. In making these examinations the physician must be cautioned not to attempt them without consent of the party concerned, even though ordered so to do by the court. Refusal to submit to an examination is probable evidence of falsity of the alleged charge, although in several cases courts have held that, in an action for divorce on the ground of impotence, the court had power to compel submission by the plaintiff or defendent to a surgical examination.[2]

In establishing proof of impotence, the question involved is impotence as regards the other party to the marriage contract. There is no question as to the capacity for intercourse with others, but simply the question of capability with the married partner. Not only coitus but a proper and complete coitus is expected, so that each case must be determined upon its own merits.

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[1] "Marriage and Divorce", in *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 1909, **3**, 783.

[2] See Devenbagh *v.* Devenbagh, 5 Paige, 558: Le Barron *v.* Le Barron, 35 Vt. 365.

CHAPTER XI

PREGNANCY: SIGNS OF DELIVERY

Conception depends upon the union of the male and female sexual elements, so that pregnancy is possible whenever the spermatozoa find their way into the vagina, although for reasons previously mentioned fecundation may not occur. This union of the sexual elements usually occurs in the uterus, although it may take place in the Fallopian tubes, ovary, or even in the abdominal cavity.

Every normal woman is capable of conception during her active sexual life, which is supposed to continue from the time of appearance of menstruation until its cessation. Ordinarily the menstrual flow (catamenia) is established between the ages of fourteen and sixteen, although it may occur much earlier or not appear until much later. Thus, cases are reported of the establishment of menstruation a *few days after birth*, and at the ages of 1, 2, 3, 4, and 5 years; while its first appearance has been reported at the ages of 30 and 47.[1] Once established, the menses appear periodically as a rule every 28 days, although many women show more or less irregularity in this respect. The average age at which the function of menstruation ceases is from 40 to 50 years, although it may continue up to 66, 69, 75 and in one case, quoted from Orfila by Taylor, up to 99 years of age. It will be seen, therefore, that an absolutely definite age for the "menopause" cannot be stated.

While the procreative power is not generally supposed to exist before the commencement of menstruation, yet the previous occurrence of menstruation is not indispensable to pregnancy, as is evidenced by the many cases of pregnancy in women who have never menstruated. While the cessation of the function of menstruation usually means the end of the period of fertility, yet it must be recognized that pregnancy may be possible after this "change of life" occurs, as fertility depends more on the integrity and activity of the ovaries than on any relationship between such activity and menstruation.

There appears to be reason for believing that impregnation is more likely to occur immediately after the termination of a menstrual period than at any time during the interval between periods, although there is no period in the menstrual interval at which impregnation may not occur. The basis of this idea is that ovulation (bursting of the Graafian follicles with the throwing off of ova) is regarded as coincident with menstruation. In this connection von Hofmann says "According to the experiences of obstetricans most conceptions occur in the first days after cessation of menstruation. During the World War opportunity was afforded of testing the theory that the capability of conception of women was a variable factor during the menstrual intervals. Owing to the short furloughs of the men in the field, cohabitation and the time of conception could be fairly accurately fixed. In a series of cases it could be determined that the possibility of conception of the women increased immediately after the end of menstruation, reached its high point about 6 days after the beginning of menstruation and remained so up to the 12th or 13th day, and then sank. Conceptions in the last 6 days before the appearance of the next menstrual period (pre-menstrual period) were rare, although they were found to be possible in this period."[1]

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[1] Taylor, *Medical Jurisprudence*, 12th Amer. Ed. 1897, p. 663. See, also, Gesell, Jour. Amer. Med. Assoc., 1928, **90**, 840.

It must be stated that sexual intercourse is not essential for the liberation of the ovum, as this latter process occurs whether or not there has been coitus. However, it must be admitted that the sexual orgasm may cause the rupture of the Graafian follicle and the discharge of the ovum into the tubes. While menstruation and ovulation may be more or less coincident, yet these phenomena are not mutually dependent. As Edgar[2] states: "Without going into the argument on either side, we may now accept the statement as a fact that menstruation and ovulation may occur independently of one another. Women menstruate after the ovaries are removed, and on the other hand impregnation has occurred in women who have never presented any of the phenomena of menstruation, showing that ovulation must have occurred in the absence of menstruation."

Given a fertile ovum, discharged from the ovary into the Fallopian tubes, a union with fertile spermatozoa is necessary before pregnancy can begin. The question arises here as to how long, after insemination occurs, do the spermatozoa retain their active motility and their fecundating power.[3] Bischoff and Valentin showed that spermatozoa retain their vitality for as long as 7 days within the body of a woman, while Haussmann found in the cervix of a woman 7½ days after the last coitus virile spermatozoa, and Bossi finds that spermatozoa retain their vitality for at least 17 days, even through a menstrual period. As the time necessary for the ovum to make its descent along the Fallopian tubes varies and as the motility of the spermatozoa is necessary to permit of its movements through the vagina into the uterus and, possibly, even into the ovary before impregnation of the ovum occurs and implantation takes place, actual conception is by no means to be regarded as simultaneous with insemination. Impregnation from a single coitus may take place within a few hours or may occur at any period during the viability of the spermatozoa within the genital tract, that is within 7 days, or, if we take the figures of Bossi, within 17 days.

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[1] *Lehrbuch der gerichtlichen Medizin.*, Elfte Auf., umgearbeitet von Haberda, 1927, S. 182.

[2] "Pregnancy, Labor and the Puerperal State" in *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 1907, **2**, 511. See also Novak, Jour. Amer. Med. Assoc., 1930, **94**, 833.

[3] See Moench, Jour. Amer. Med. Assoc., 1930, **94**, 478.

Precocious Pregnancy.—By this is meant the occurrence of pregnancy at a very early age. Probably the earliest case of pregnancy recorded is that of Lefebere[1] of a girl born with hair on the pubes, who menstruated at the age of four and became pregnant when *eight* years of age. Likewise, cases of pregnancy with delivery of living children have been reported in females of eight years and ten months, nine years, ten, eleven, and twelve years of age, while there are many such cases in girls of fourteen. It will be observed that, in all of these cases of early pregnancy, there was very early menstruation.

Late Pregnancy.—While, as we have seen, a woman over fifty-five may generally be regarded as past the child-bearing age, yet each case must be a law unto itself. It is not especially uncommon to learn of pregnancies between 50 and 60. "Halles records a labor occurring in a woman seventy years of age, and another in a woman of sixty-three years. Another physician records the birth of twins in a woman sixty-four years of age."[2] The older a woman is at the time of marriage, the longer deferred is the age at which she becomes sterile. The younger married women have a longer chance for fertility but this ceases at an earlier age than it does with those married late.

Duration of Pregnancy.—To fix an absolutely definite period for utero-gestation is practically impossible, because we have no exact data as to the time when a specific pregnancy actually began. Not only must the ovum be fertilized by union with the spermatozoon but this fertilized ovum must be implanted within the body of the female, usually in the uterus but occasionally extra-uterine. Further, the period of gestation is not an invariable one, being different in different women and varying in different pregnancies in the same woman. However, it is important that we have some general idea as to the normal average duration of pregnancy as well as to the extent to which this period may be extended or shortened and yet a living and viable child be born.

By the duration of pregnancy we mean the period which elapses between actual impregnation and the beginning of labor. Probably, as Jaggard states, the real duration of pregnancy in the human female is an unknown quantity. There are but two factors, which may permit an approximate estimation of the duration of pregnancy, and both of these are open to error, namely the date of menstrual suppression and the date of a single coitus.

Cessation of Menstruation.—As is well-known, when pregnancy occurs, the menstrual periods stop, in the vast majority of healthy women, until a variable time after delivery has taken place. However, it is to be recalled that some women in whom these periods have never appeared have become pregnant, while other women may menstruate for several months after pregnancy has occurred. Such irregularities make it impossible, of course, to determine anything about the time of beginning the pregnancy in such women. Thus, Taylor cites a case of a woman who menstruated up to within two months of her delivery. Further, it must be remembered that the menstrual flow may cease from many causes other than pregnancy, so that there is much uncertainty in a given case of amenorrhea as to its exact significance. It is important, therefore, that the physician be somewhat cautious in his statements and not say too definitely that the woman must be pregnant because the menses have stopped or that she cannot be pregnant because the menstrual flow continues. However, the cessation of menstruation is so commonly known as an accompaniment of pregnancy that it is not infrequent to find women *feign menstruation* in order to conceal an illegitimate pregnancy.

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[1] Med. Press and Circ., 1868, p. 245. Cited by Tidy, *Legal Medicine*, 1884, **3**, 52. See, also, "Precocious Pregnancy" by Dittrick, Jour. Amer. Med. Assoc., 1927, **88**, 722.

[2] See Dorland, "The Legal Aspects of Pregnancy", in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **I**, 943.

Experience has shown that the average, apparent duration of pregnancy is ten lunar months (nine calendar months in popular reckoning), forty weeks, or 280 days from the beginning of the last menstrual period. It is probably true that in the majority of cases labor comes on at the date when the tenth menstruation would have begun, had it not ceased at the beginning of the pregnancy. On such a basis the duration of pregnancy would be reckoned as including ten menstrual cycles of the specific woman in question. However, this method can not be adopted for those who are more or less irregular in their menstrual cycle or for those who have a short or a long interval between periods.

In reckoning the duration of pregnancy from the beginning of the last menstrual period, it is, of course, not possible to know whether the ovum impregnated was discharged at the time of the last menstrual period, or in the intermenstrual period, or at the beginning of the next period. Thus, an error of practically a full menstrual cycle might obtain, depending on the time of discharge of the ovum which was impregnated. Murray[1] records a case in which insemination occurred about 2 hours before menstruation began and was followed by pregnancy and labor in 272 days. There was no previous intercourse for over two months prior to this period and no coitus subsequent to the fruitful one. The menstrual period following this intercourse was a perfectly normal one, so that the case might very well be regarded by the woman as one of gestation protracted one month. Admitting that we have errors in this method of computation of the period of gestation, the best we can do is to compute 280 days (forty weeks) from the beginning of the last menstruation, under which conditions we will arrive at a date which is about the middle of the fortnight in which the labor will occur.

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[1] Edinburgh Med. Jour., 1892, **38**, 201.

Duration From a Single Coitus.—As we have previously stated, the spermatozoa retain their virility in the genital tract of the woman for at least seven days and possibly as long as seventeen, so that impregnation of the ovum may occur at any time within such a period of virility. For this reason we cannot regard the time of insemination as necessarily coincident with impregnation, although the case previously cited from Murray might indicate impregnation within a very short time, even though the spermatozoa had to make their way into the uterus against the menstrual flow and reach the Fallopian tube in time to fertilize the discharged ovum. However, there must be an uncertainty of the interval between intercourse and impregnation in any case, as the conditions upon which fertilization of the ovum may depend will not always be the same. The computations of various obstetricians as to the duration of pregnancy, dating the beginning from the date of a single coitus, lead to the average figure of 272 days. However, there is much variation in the figures obtained in these studies. Thus, Reid, in 40 cases, found the duration running from the 260th to the 294th day after intercourse, while Montgomery, in 56 cases, reports the pregnancies as occurring on the 242nd to 301st day following the fruitful coitus, 22 of this number being delivered between the 274th and 280th days. While 272 days may be regarded as the average duration of pregnancy, dating the period from the time of a single coitus, yet, as the figures of Reid and Montgomery show, we may have a variation of at least a month from this average figure, a variation which coincides with the possible difference in time at which the ovum may be impregnated. Hence, it will be seen that by this method of reckoning, also, the duration of pregnancy is far from an exact period. As Taylor remarks: "We must, therefore, be prepared to admit, either that conception may in some cases be delayed for so long a period as from five to seven weeks after intercourse, or that there may be a difference of from five to seven weeks in the duration of pregnancy. Whatever may be the explanation adopted, it is obvious that, in a medicolegal view, the only conclusion at which we can arrive is that the period of gestation in woman is *not*, as it was formerly supposed to be, a fixed and invariable term."

Protracted Gestation.—That pregnancy may be protracted beyond the average period of 280 days, dating from suppression of menstruation, or 272 days, reckoned from the date of a single intercourse, is evident from the various reports found in the literature. It is, of course, possible that some of these cases are inaccurately reported, inasmuch as the exact period of impregnation cannot be positively stated, yet many authentic cases of prolonged gestation (*partus serotinus*) do occur and the fact is recognized by the laws of many countries and in our country and in England courts have ruled as to the legitimacy of certain periods of gestation. Thus, in Scotland, France, and Italy, legitimacy is allowed if the birth is not more than 300 days from the cessation of menstruation; in Germany a period of 302 days is permitted; in Austria 307 days;

in England the courts have declared a birth legitimate 331 days after the last coitus[1]; while in America pregnancies lasting 313 and 317 days respectively have been declared legitimate.[2]

Without attempting to cover the cases reported in the literature concerning protracted gestation, we will mention a few cases for reference. Thus, Acker[3] reports a pregnancy lasting 305 days; Pürkhauer[4] one of 316 days; Hames[5], 320 days; Taussig,[6] 323 days; Murray,[7] 330 days; Resnikow,[8] eleven months; Schlichting,[9] 334 days; Holland,[10] 340 days; Miller,[11] twelve months; and Wilson,[12] 371 days.

In cases of prolonged gestation, the chief matter of evidence, when the question of legitimacy is raised, is the latest possible date of access of the husband, such a point being ordinarily fixed by the husband's death, by such severe illness as would preclude coitus, or by the date on which he left home for a protracted stay. It must be admitted that, in many of these cases of very long protraction of pregnancy, the exact time of impregnation is uncertain so that one is not in a position to decide for himself, but must base his opinion largely on the statements of the woman as to the probable beginning of the pregnancy. The question raised in these cases of disputed legitimacy is whether or not the interval between the date of access and that of delivery is consistent within the possibility of the husband or the party accused being the father of the child. While evidence in such cases is allowed as to authentic reported cases of protracted gestation, yet it must be remembered that by no means in all of these reported cases is the history of the case so clear as to warrant an absolute statement that impregnation occurred at a definite time.

Diminished Duration of Gestation.—The point involved here is whether or not the period of utero-gestation may be diminished and yet a living child be born. Probably this is a more frequent occurrence than is protracted gestation. While in cases of protracted gestation the children are not, as might be expected, much more developed than are those born in the usual period, yet in cases of short duration of pregnancy the development of the child has a definite relation to the period of uterine existence.

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[1] Gaskill *v.* Gaskill, Probate, Divorce and Admiralty Division, July 24, 1921. See Brit. Med. Jour., 1921, **2**, 220; Jour. A. M. A., 1921, **77**, 716.

[2] Commonwealth *v.* Hoover, 3 Clark, Pa. 514. (313 days). Commonwealth *v.* Porter, Tried in Jan. Term 1844, Cambria County, Pa. See Amer. Jour. Med. Sci., 1845, **36**, 338 (317 days).

[3] Amer. Jour. Obs., 1889, **22**, 1276.

[4] Fried. Bl. f. ger. Med., 1890, **41**, 191.

[5] Lancet, 1901, **I**, 1496.

[6] Amer. Jour. Obs., 1901, **44**, 516. Alons, Nederl. Tijdschr. v. Geneesk., 1924, **2**, 3011. (322 days).

[7] Brit. Med. Jour., 1889, **I**, 282.

[8] Centralbl. f. Gynäk., 1894, **18**, 575.

[9] Arch. f. Gynäk., 1880, **16**, 210.

[10] Brit. Med. Jour., 1902, **I**, 659.

[11] Practitioner, 1916, **100**, 94.

[12] Univ. Med., Mag., 1890, **2**, 515.

Of further importance in this connection is the period of gestation necessary to produce a living child. As Tidy remarks: "This question involves matters of grave importance, affecting not only the legitimacy of children, but the honour of parents, and sometimes even the interests of nationalities." It is important that we distinguish here between a living and a viable child. It is, of course, evident that a viable child must be living, but a living child or fetus may not be viable. In relation to a living child all that is necessary to determine is some sign of life, such as the movement of single muscles, such as wrinkling of the skin, opening the mouth, moving of the head or hand, etc. it not being essential that the child cry or breathe. By viability is meant capability of surviving.

It is generally accepted that a child is not viable before the end of the seventh lunar month, although apparently authentic cases are recorded of children born between the fifth and sixth months of gestation having reached adult age.[1] While a living child may be born between the fourth and fifth months, such do not live longer than a few hours.

The characteristics of the child at different periods of development are fairly well marked, and should be familiar to the student from his study of embryology. The nearer one approaches to the full period of gestation, the more difficult it becomes to determine the exact age of the child. There would probably be little difficulty in determining that a child was about 7 months old, but it might be rather difficult and risky to state definitely that a given child was eight instead of nine months old, as the development might be somewhat delayed or accelerated as the case might be. The point involved here is that if a child is born with signs of seven month's development at about nine months from the last possible access of the husband of the woman, it would be exceedingly strong evidence of the illegitimacy of the child. Much depends, in such cases, on the statements of the woman as to the time of cessation of her menses, and she may have much reason to prevaricate about this. The husband may have raised the point of legitimacy, stating that his last access was not within a period permitting of such a pregnancy. Under such circumstances the work of the medical jurist is quite different from that of the practitioner to whom a woman comes in the course of an ordinary pregnancy, as the former must be prepared for lies and deception in these matters as the woman may have much to conceal. As Beck[2] remarks: "It may be deemed *barely* possible that a child born at seven months may *occasionally* be of such a size as to be considered mature, yet I apprehend that the assertion is most frequently made by those whose character is in danger of being destroyed." So, also, in cases where coitus has occurred prior to marriage, the question of legitimacy may be raised where a mature child is born seven months after marriage. Sound advice on such points has been given in the following words, quoted by Tidy, "Take care not to be deceived. I have known many remarkable cases of fully developed and mature children being born within seven months of marriage. They are commonly regarded as marvels; but in my experience they are marvels limited to first pregnancies."

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[1] See De Lee, *Principles and Practice of Obstetrics*, 4th ed. 1924, p. 118, who reports personal delivery of a viable child 182 days after the day of conception.

[2] *Medical Jurisprudence*, 10th ed. 1850, 1, 580.

On the other hand, because a full-term child is small and may resemble in size and weight a seven or eight months' child, one cannot advance this as proof of illegitimacy. There is, as is well-known, just as much difference and variation in size and development of newborn children as there is in children of more advanced age. Some women invariably give birth to small children, while others always have large sized progeny. This may not have any relation to the size of the mother, as many robust women have small children and many small women large children.

We cannot attempt to point out here the characteristics of the development at different periods of uterine life. The medical jurist will often be called upon to state the approximate age of a child and to state whether or not, in his opinion, the child is of an age consistent with possible pregnancy following intercourse at such a date. Probably the most reliable points in this connection are the length of the child, the weight and the diameter of the head. These three taken in connection with the appearance of the center of ossification in the lower epiphysis of the femur and certain general points will usually solve the question as to whether the child is of full term. For a discussion of such factors works on embryology or obstetrics should be consulted.

Feigned Pregnancy.—Pregnancy has been sometimes feigned for the purpose of extorting charity, for compelling marriage, or for the purpose of obtaining an inheritance. It will be necessary in such cases to use extreme care to detect the imposture and to make a very thorough physical examination of the woman. For some reason these impositions are more frequently allied to advanced stages of pregnancy, so that careful examinations will usually reveal the fraud. In most cases it is easier to prove that a women is not pregnant than that she is. In such cases all sorts of deceit will be practiced and the story of the woman may sound plausible, but careful attention to the absence of definite signs of pregnancy will clear up the case, as the woman cannot simulate the more decisive signs of pregnancy although she may be able to feign the doubtful ones. The physician should not accept the statements made to him as true but should make his opinion rest entirely on the result of his physical examinations. A refusal on the part of the woman to permit the examination will, usually, be sufficient basis for declaring her an impostor. Feigning of pregnancy is today, perhaps, less frequent than is the concealment of pregnancy, as in the latter case the woman, usually a young girl, does not care to have the matter known. It is such cases as these that are brought to the attention of the physician in connection with requests for abortion, of which we will speak later.

Impregnation during Unconsciousness.—The question has not infrequently been raised in courts of law as to whether or not it is possible for a woman to become pregnant without her knowledge. It is undoubtedly true that coitus might occur during very deep sleep from some pathological cause, but it is hardly conceivable that a woman should be unaware of the act if attempted during ordinary sleep. Many cases are known where intercourse has taken place when the woman was under the influence of alcohol, narcotics, or anesthetics, or where the sexual act has occurred during hypnotic sleep. In such cases impregnation is of course possible. As a rule these cases are associated with the question of rape.

While the sexual congress may not have been a matter of the knowledge of the woman, especially if she be a married woman, yet it is difficult to believe that she should be unconscious of her condition after the lapse of a few months, as the suppression of the menses and other signs should make her suspicious and lead her to consult a physician, unless she be a woman of very low intellect indeed. If the woman be a virgin, the local soreness and possible injuries to the vagina and vulva resulting from the first coitus should lead her to suspect that she had been violated.

Unconscious Pregnancy.—This condition is quite distinct from the preceding. Here we have to consider the question as to whether a woman may be unconscious of her pregnancy, although she is perfectly aware of the fact that coitus has occurred. In married women who have had no children for many years or in those who conceive very late in life, it is possible to imagine a gestation advancing quite well along without a knowledge on the part of the woman of the pregnancy. The symptoms are ascribed to some pathologic condition rather than to pregnancy, and much surprise is often shown when the woman is told of the condition actually present. In some cases there may be distinct motives for pleading an ignorance of these conditions, so that very careful examination is necessary. It has been stated by women, who have been accused of infanticide, that they did not know they were pregnant and that the delivery of the child was sudden and unexpected by them. Such cases are probably unworthy of belief. Unmarried women occasionally consult a physician in the hopes that he may help them out of a difficulty, knowing full well that they have exposed themselves to pregnancy. It certainly must be a rare situation if a women would be unconscious of her pregnancy after the middle period of gestation.

Superfetation.—By this term is meant the fertilization of a second ovum when there is another fertilized ovum undergoing development in the uterus. The result of such a condition, if possible, is two fold: First, two children may be born at the same time but differing in development; second, two children of equal development are born at different times, the periods of their birth varying several weeks or months. This term should not be confused with that of *superfecundation*, which means the impregnation of one or more ova after one has already been impregnated or the fertilization of one or more ova of the same ovulation at a second coitus. The result of superfecundation is multiple pregnancies and the children may or may not differ according as they may or may not have had the same father. There are cases in which a woman has given birth to twins, one white and one black, the result of coitus with a white man closely following that with a black.

That superfetation is possible, even probable, must be admitted, while cases of superfecundation are far from uncommon. With superfetation, however, it must be remembered that ovulation must occur some time after the fertilization of the first ovum, if this condition is to be regarded as possible. Ordinarily ovulation ceases during pregnancy, but it cannot be absolutely assumed that it may not occur at this time. We know that menstruation and ovulation are not interdependent, so that because one ceases the other need not; and menstruation does not cease in all women during the early months, at least, of pregnancy.

While the actual occurrence of superfetation may be regarded as possible, yet such occurrences as are included under that heading may be explained by the assumption of twin pregnancies, in which one of the twins has developed to a greater extent than has the other. It is a well-known fact that the two children in twin pregnancies rarely show equal physical vigor, so that in such cases as we are discussing here this lack of development of one twin may lead to the assumption that this child was of seven months, while the other may represent a normal nine months' child. Or, where one of normal development is expelled at term, the other child remains in utero until it is fully developed. Some writers believe that the reported cases of alleged superfetation are cases of pregnancy occurring in a double uterus, one ovum being fertilized in either uterus at successive coitions.

It has been shown by Bonnar that the earliest date after confinement when a woman may again become pregnant is 14 days, so that a second child might be born within about 9 months of another, but this would not be in any sense a case of superfetation.

The Signs of Pregnancy.—The medical jurist may be called upon under different conditions to determine whether or not pregnancy exists in a definite case. It is to be repeated here that the physician should never examine the woman without her consent, as by so doing he incurs the possibility of a charge of assault.

The signs of pregnancy are both subjective and objective, only the latter being trustworthy from the medicolegal viewpoint, as the woman may deliberately deceive the physician or she may actually be deceived herself. She may be so desirous of becoming pregnant that she easily believes that her subjective signs are definite evidence of this condition, or, on the other hand, a woman who has indulged in illicit intercourse may become so fearful of the result that she imagines that she is pregnant. This constitutes the condition known as pseudocyesis or phantom pregnancy.

"It is well to note that a pregnancy may be *presumptive*, it may be *probable*, or it may be *certain*. It is presumptive when, without any expert investigation, the woman, having been exposed, legitimately or illegitimately, to the possibility of conception, presents some or all of the subjective signs of pregnancy, together with a minor degree of abdominal enlargement. It is probable if these signs steadily increase in intensity and other signs develop at proper periods, which in a typical case of gestation should be superadded to the initial symptoms. Finally, a pregnancy is certain only when there are present the so-called positive or diagnostic signs of pregnancy, variously estimated as from three to five in number. They include the fetal heart sounds, the fetal movements, ballotment, vaginal and vulvar discoloration, and intermittent uterine contractions."[1]

For the uterine, vaginal, abdominal and general signs and symptoms of pregnancy we refer to works on obstetrics, as space does not permit their discussion. It is to be said that the examining physician must make certain of the presence or absence of pregnancy in a medicolegal case, as the many legal points will depend to a large extent on the accuracy of his examinations.

SIGNS OF DELIVERY

Delivery is a subject which probably requires more frequent medicolegal attention than does pregnancy. In cases of concealment of birth, abortion or infanticide, and where questions involving supposititious children are concerned, it becomes necessary for the medical jurist to make a physical examination to determine the presence or absence of signs of delivery. The questions usually arising have reference to the suspicion of a positive pregnancy and delivery, and such points may oftentimes be somewhat clarified by information gained either from the subject herself or from friends or those about her. Of course, where there is an attempt to conceal the situation, the woman will deny any such condition and few of her associates will known any thing about it.

Signs in the Living.—The certainty with which questions bearing on delivery may be answered will depend upon the time that has elapsed since the parturition, or, if the gestation has not reached its full term, on the time of the delivery with reference to the stage of fetal development. In the narrow obstetric sense the discharge of the ovum at any time during the first 3 months of pregnancy is known as an abortion; between the 3rd and 6th months it is styled a miscarriage; and between the 6th and 9th months a premature labor. However, in law there is no such distinction, the expulsion of the ovum, fetus or child at any period of gestation being known as abortion.

The signs of delivery are distinct in proportion to the maturity of the ovum. If the abortion take place between the second and third months, there may be no signs whatever, so that the examiner would be forced to depend to a large extent on an examination of the uterine scrapings for decidual cells. Here, however, the examination must be made within a very few days if any information of value is to be obtained. Later than the third month, the signs of delivery may be slightly clearer, but nothing definite may be obtained unless the examination be made promptly. Possibly there may be some congestion of the vulvar tissues, the cervix uteri may be found enlarged and soft and more or less funnel shaped, while the patient may show more or less weakness due to loss of blood. Search for the presence of membranes or decidual cells in the uterine scrapings should be made.

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[1] Dorland, "The Legal Aspects of Pregnancy", in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, I, 929.

At term the signs of delivery are more pronounced and longer in duration, but little is to be expected even in such cases unless the examination be conducted within a week, or at most ten days. These signs at term may be summarized as follows: The woman is usually weak, the countenance pale, there is a dark areola around the eyes, and there is general indisposition with a quickened, soft and compressible pulse. The value of such findings is of importance only when they have occurred suddenly while the woman was in previous good health, especially if pregnancy was known or suspected. The breasts will be enlarged, full, possibly nodulated, the nipples enlarged and the areolae and pigmentation about them more or less pronounced, and milk (colostrum) is almost certain to be present. The skin of the abdomen will be relaxed, flaccid, and sometimes thrown into folds. Numerous light colored shiny streaks (*lineae albicantes*) may be seen on the abdomen and thighs. The viscera may be easily palpated through the abdominal wall, and the uterus may be felt as a large hard body reaching well above the symphysis pubis, especially if the examination be made within a week after delivery. This condition of the abdominal walls is of value, only if taken with the changes in the breasts and genital organs, as any disease which has caused enlargement of the abdomen may give rise to a similar appearance. The generative organs are relaxed, more or less swollen and contused, with blood about them. The outlet is dilated, the vagina is smooth, relaxed and enlarged and may show recent tears. The perineum may or may not show lacerations. The cervix is enlarged and shortened, the internal os gradually closing if all the uterine contents are extruded and the external os remaining patulous for some days and, possibly, showing lacerations on one side. The body of the uterus is enlarged from two to four times the size of the uterus in the unimpregnated state, the actual size depending upon the time that has elapsed since the birth. Soon after delivery a discharge, known as the *lochia*, appears, which may disappear after the third day, but usually lasts for 1 to 2 weeks. In the first few days this discharge is red in color and is known as the *lochia rubra*, later it becomes serous and is styled the *lochia serosa*, and finally becomes yellowish or even greenish in color (*lochia alba*).

The signs above mentioned are found only when the examination is made more or less promptly after the delivery. Many women resume their natural state more promptly than others, so that even soon after delivery in such women many of these signs will not obtain. In others, however, proofs of delivery may be obtained for 2 or even 3 weeks. However, it is wise to make the examinations as soon as possible in every case, in order that as much information as possible may be forthcoming. Probably all of the signs mentioned, with exception of the uterine enlargement and the presence of tears or lacerations, will have disappeared, in most cases at least, in ten days to two weeks.

Oftentimes it becomes necessary to attempt to determine how long a time has elapsed since the birth, especially where there may be a question of abortion or infanticide. It may be said that an opinion becomes difficult after 8 to 10 days, while after two or three months it is legally regarded as impossible to assign the date of birth with any degree of precision, especially in primipara.

In a case of pretended delivery, contested legitimacy, or disputed maternity, the point may be raised as to whether or not the woman has at any previous period of her life given birth to a child. Such a question can be answered only with reference to delivery at term, as there may have been early abortions which show no fixed signs. There are certain signs which may be taken as more or less certain proofs of previous pregnancies. These may consist of a more or less flaccid condition of the abdominal walls with the presence of the lineae albicantes in most women, Mann[1] asserting that in about 8 per cent of cases these lines are wanting. The breasts will not be firm and protuberant, as in virgins, but softer and pendulous; the nipples will be larger and more prominent and there will be greater discoloration about the nipple. The vulva will be patulous, the labia relaxed, the hymen absent, the rugae of the vagina obliterated. In a woman who has not born children the mouth of the womb is in the form of a slit and the angles are bent down, while in a woman who has born children the mouth becomes elongated and loses the bend at its extremities.

In this connection it should be mentioned that the presence of an intact hymen is no evidence that the woman has not been pregnant and may not have had an abortion in the early days of pregnancy.

Signs in the Dead.—In instituting inquiries relative to previous pregnancy in a dead body, the history of the case may furnish valuable information, but this cannot be taken as conclusive. The same difficulties arise here as in the living, if the pregnancy was of recent or remote origin. If death took place after some time had elapsed since delivery, most of the signs of pregnancy will be lacking. If the abortion has occurred at a very early period of the pregnancy, almost nothing can be determined from examination of the local organs. Curettage of the uterus may furnish shreds that will show decidual tissue and thus make possible a diagnosis. After the third month the placental site in the uterus can be distinguished as a raised and reddened area and placental debris may be obtained.

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[1] *Forensic Medicine and Toxicology*, 1893, p. 118.

If the woman has been recently delivered at term the following signs will be found. The uterus is large, flaccid and hemorrhagic, will be from 9 to 12 inches long, and from 6 to 8 in width; the internal os is patulous, and the cavity will contain decidual debris and blood. Where the placenta was attached the organ appears exposed presenting several large openings of the uterine sinuses. The cervix is thin and elongated and often shows ecchymotic spots. The signs previously mentioned in the lower genital organs will, of course, obtain here. The Fallopian tubes and ovaries are congested and have a purple color. Corpora lutea may be found in the ovary, but these can not at present be regarded as having any great diagnostic significance.

CHAPTER XII

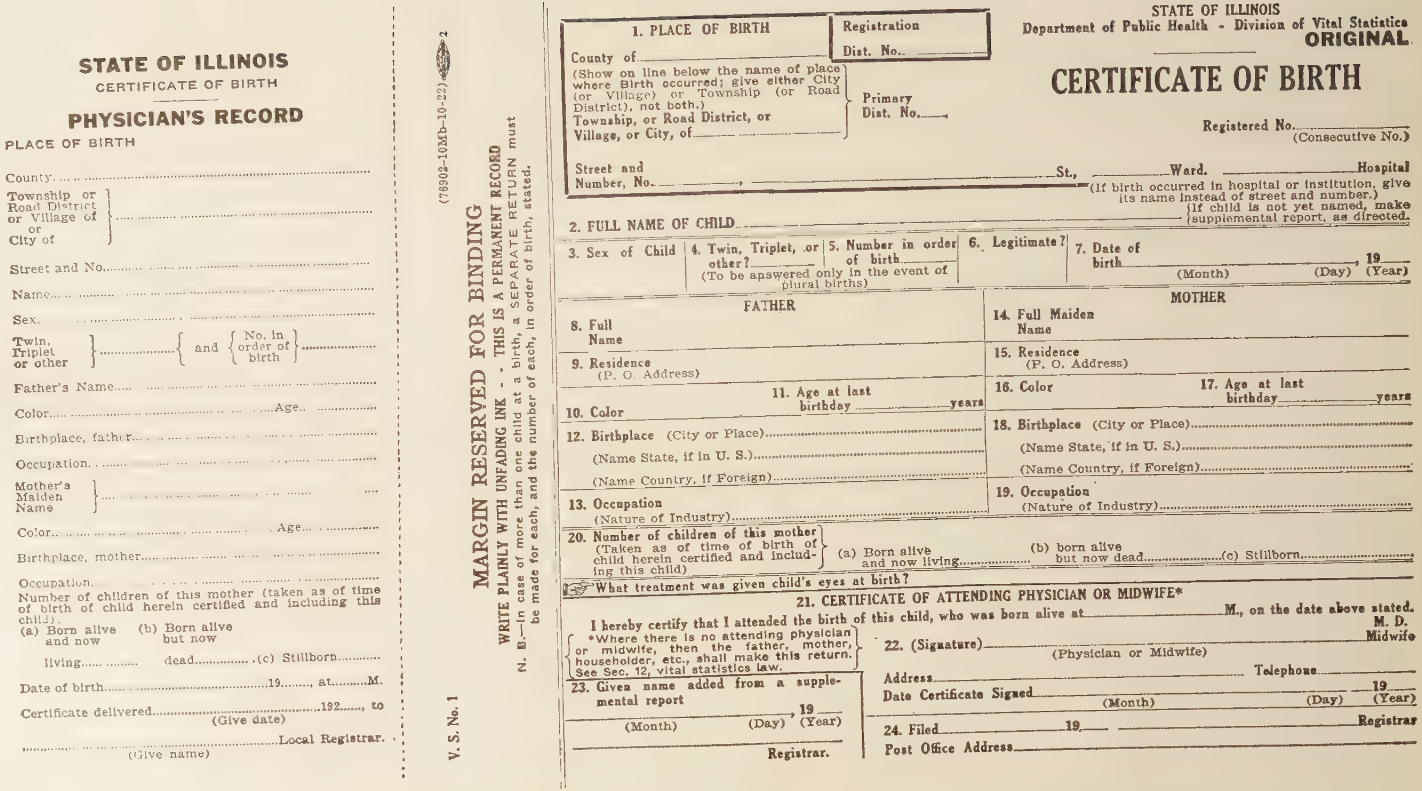
BIRTH: INHERITANCE: LEGITIMACY: PATERNITY AND AFFILIATION

Birth, in the legal sense, means the complete delivery of the child. In other words, the child must be *completely* without the body of the mother, although the umbilical cord need not have been separated. In law, the presumption is that all children are born dead unless it can be shown that they were actually born alive. To constitute a *live birth*, from the legal point of view, all that is necessary is the presence of some sign that may be associated with life. Thus, the pulsation of the child's heart, or of one of its arteries, or the slightest voluntary movement, such as the wrinkling of the forehead, opening of the mouth or eyes, the movement of a limb, etc., will legally prove a live birth. It is not at all necessary that the child breathe or cry to constitute a live birth in America or England, although in Scotland and Germany crying is held to be essential and, in France, respiration, to constitute live birth.

Although legally all children are born dead, that is the existence of life must be proven should questions arise, a child is medically *dead-born* when there is no sign of life as manifested by lack of circulation or respiration, and *live-born* when there is any sign of life after it is completely born. A child is *still-born* if it is live-born but makes no attempt to breathe and finally dies without respiration having been established.

Date of Birth.—Evidence is not infrequently demanded as to the date of birth in cases of alleged attainment of majority, in cases of inheritance, in questions of contested legitimacy, and in disputed succession. The time of birth is the moment when the body of the child is completely extruded from the body of the mother, and this exact time should be recorded by the attending physician, as the rights of the child if he survive or of others if he die may be greatly affected by this time of birth. Thus, a person attains his legal majority the first instant of the day before the 21st anniversary of his birth, the law assuming that part of a day is equal to a whole day in a legal sense. While it may make little difference, under ordinary circumstances, whether the birth is recorded as being at 11:59 midnight or 12:01 A.M., yet just this lack of noting the exact time of birth may deprive an individual of an inheritance at his majority or may invalidate a will, which became effective only at his majority.

For many civil purposes it is often necessary that a person be able to establish the fact of his birth at a certain time and this he can do only when there is some record of such occurrence. The old practice



STATE OF ILLINOIS
CERTIFICATE OF BIRTH
PHYSICIAN'S RECORD

PLACE OF BIRTH
County.........
Township or Road District or Village of or City of ....
Street and No.........
Name.........
Sex.........
Twin, Triplet or other .... and No. in order of birth ....
Father's Name.........
Color......... Age.........
Birthplace, father.........
Occupation.........
Mother's Maiden Name.........
Color......... Age.........
Birthplace, mother.........
Occupation.........
Number of children of this mother (taken as of time of birth of child herein certified and including this child).
(a) Born alive and now living......... (b) Born alive but now dead......... (c) Stillborn.........
Date of birth.........19........, at.........M.
Certificate delivered.........192......., to (Give date)
.........Local Registrar. (Give name)

(78902-10Mb-10-22) 2

V. S. No. 1

MARGIN RESERVED FOR BINDING
WRITE PLAINLY WITH UNFADING INK - - THIS IS A PERMANENT RECORD
N. B.—In case of more than one child at a birth, a SEPARATE RETURN must be made for each, and the number of each, in order of birth, stated.

STATE OF ILLINOIS
Department of Public Health - Division of Vital Statistics
ORIGINAL

CERTIFICATE OF BIRTH

1. PLACE OF BIRTH
County of.........
(Show on line below the name of place where Birth occurred; give either City (or Village) or Township (or Road District), not both.)
Township, or Road District, or Village, or City, of.........
Registration Dist. No.........
Primary Dist. No.........
Registered No......... (Consecutive No.)
Street and Number, No........., ...St., ...Ward. ....Hospital
(If birth occurred in hospital or institution, give its name instead of street and number.)
2. FULL NAME OF CHILD......... (If child is not yet named, make supplemental report, as directed.)
3. Sex of Child | 4. Twin, Triplet, or other?......... | 5. Number in order of birth......... (To be answered only in the event of plural births) | 6. Legitimate? | 7. Date of birth......... (Month) (Day), 19... (Year)

FATHER
8. Full Name
9. Residence (P. O. Address)
10. Color
11. Age at last birthday.........years
12. Birthplace (City or Place).........
(Name State, if in U. S.).........
(Name Country, if Foreign).........
13. Occupation (Nature of Industry).........

MOTHER
14. Full Maiden Name
15. Residence (P. O. Address)
16. Color
17. Age at last birthday.........years
18. Birthplace (City or Place).........
(Name State, if in U. S.).........
(Name Country, if Foreign).........
19. Occupation (Nature of Industry).........

20. Number of children of this mother (Taken as of time of birth of child herein certified and including this child) (a) Born alive and now living......... (b) born alive but now dead......... (c) Stillborn.........
☞What treatment was given child's eyes at birth?

21. CERTIFICATE OF ATTENDING PHYSICIAN OR MIDWIFE*
I hereby certify that I attended the birth of this child, who was born alive at.........M., on the date above stated.
*Where there is no attending physician or midwife, then the father, mother, householder, etc., shall make this return. See Sec. 12, vital statistics law.
22. (Signature)......... (Physician or Midwife) M. D. Midwife
Address......... Telephone.........
Date Certificate Signed......... (Month) (Day) 19... (Year)
23. Given name added from a supplemental report .... (Month) (Day), 19... (Year)
.........Registrar.
24. Filed.........19.........Registrar
Post Office Address.........

of recording births in the family bible still obtains in some sections, but difficulty arises in finding the record when desired. In the early days births were recorded in church records or were left to the memory or scant records of the physician in charge. At the present time, most of our states require registration of births within a short period after birth[1] (in Illinois within 10 days). Unfortunately there is no great penalty attached to non-observance of this requirement on the part of the physician, so that physicians have become very lax in this respect. On page 211 is shown the type of Birth Certificate at present used in Illinois.

Concealment of Birth.—In cases of suspected infanticide or of birth of illegitimate children, either within or without the marriage bond, a woman may attempt to conceal the birth for obvious reasons. The laws of the various states differ as to the type of crime, if any, covered by this act. Of course, if the birth of a child can be proven and it be found dead or is missing, the mother may be charged with murder. In some states, where the law of privileged communications holds, knowledge obtained while attending a woman in confinement cannot be divulged by the physician, so that testimony from him as to a birth is prohibited, unless waived by the woman. However, although there is no crime in concealing the fact of pregnancy and of birth, in some states at least, it is regarded as a misdemeanor to adopt any secret disposition of the body. In such cases it is apparently not necessary to produce the body of the child to prove such a case, as this proof is forthcoming from the signs of delivery as obtained from the body of the mother.

INHERITANCE

It is now established in law that a child still unborn (*en ventre sa mere*) has certain legal rights in connection with all processes tending to its own benefit.[2] Thus, a legacy may be left to it; it can be made executor of an estate; or it may have various offices thrust upon it, all of which provisions, of course, become null and void if the child is dead-born. If the child is born alive, although it soon dies, it may become heir to property and such property then becomes transmissable. In this connection a recent case is of interest. A Mrs. Wells by her will created a trust fund to be divided "into as many equal parts as I may have grandchildren living at the time of my decease." One grandchild was born eight months and fourteen days after the death of the testatrix, so that the question arose as to whether this grandchild en ventre sa mere at the time of the death of the grandmother was to be regarded as living at that time. The ruling of the court was that the child was and is a living child for all purposes pertaining to her property rights under the will.[3]

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[1] See People *v.* Cramer (Mich.), 225 N. W. 595.

[2] American and English Encyclopedia of Law, 2nd ed., vol. 5, pp. 719 and 1083.

[3] In re Wells' Will (N. Y.), 221 N. Y. Supp. 714.

In America the question of inheritance is decided on a different basis from that in vogue in England. Here we do not recognize the entailing of estates or the law of primogeniture. The inheritance of individuals is usually decided on the point of minority or majority. With the male, the word minor or the state of minority is applied to any one under the age of 21 years. Such an individual, although capable of inheriting property at any age of his minority, is not placed in control of it until he reaches his majority. With the female, the age of majority is variable, being either 18 or 21 depending upon the state of residence, although certain civil functions, such as those of voting, serving on juries, etc., are not assumed until the age of 21. As to his responsibility for his acts during the period of minority, the law assumes that a child up to the age of seven is incapable of distinguishing right from wrong and is, therefore, legally incapable of crime. At fourteen the child may be assumed to have some discretion and, hence, becomes responsible for his acts.

A peculiar type of inheritance, which is prevalent in England but is found in only a very few of our states, is the so-called *Tenancy by Courtesy.* This allows the husband a life interest in the estate of the wife if she dies leaving a child born living during the life of the wife. The factors necessary to permit this type of inheritance are (1) the child must be born living; (2) the child must be born while the mother is living; and (3) the child must be capable of inheriting. In regard to live birth, we have already mentioned that all that is necessary to prove this state is some sign of life in the child. The child need not live for any stated period, as the only question involved is the delivery of a live child. Concerning the question of the birth during the life of the mother, it has been held up to recent times that a child delivered by Cesarean section or by other means after the death of the mother did not transfer this right of tenancy to the father, although such child was perfectly legitimate and was capable of inheriting in his own right. The reason for such rulings was that marriage was dissolved by the death of the mother. However, recent decisions have changed this peculiar situation, so that the father is now entitled to his estate by courtesy. With reference to the point of capability of inheriting, the law states that, if the child be a monster so deformed as to be regarded as not having human shape, it cannot itself inherit nor can the father acquire a right of tenancy. Under such conditions the estate descends to the other heirs of the wife.

LEGITIMACY

A *legitimate* child is one born in lawful marriage or within such a period after the death of the husband as is in accordance with the natural period of gestation; while an *illegitimate* child is one born out of wedlock or not within competent time after the cessation of the relationship of man and wife, or one born in wedlock where procreation by the husband is impossible, or, if born out of wedlock, whose parents do not afterwards intermarry and the father acknowledge the child. While many of the points involved in deciding such cases can be answered by medical men, yet there are usually circumstances which may indicate that the child is illegitimate, while the medical facts would be consistent with a legitimate birth.

In law every child born in wedlock or within a competent time after the marriage relationship ceases is presumed to be legitimate, unless it can be shown by competent evidence, medical or lay, that it was impossible for the husband to have been the father of the child owing to advanced age, infirmity, or absolute impotence or sterility; or that he was out of the country at the time the child must have been begotten; or that too long a period had elapsed since the last coitus; or that the husband had died at such a period as was not consistent with paternity. Further, if it can be shown that the mother had been guilty of adultery at such a period as might be consistent with the birth of the child at the date known, then the child may be deemed illegitimate, providing the child is repudiated by the husband. However, in such cases as the latter, if the husband has had access to the wife during such a period, the courts are slow to declare the child illegitimate without strong evidence of repeated adultery, as the evidence of illegitimacy must be clear and decided in order to disturb the presumption of legitimacy. Moreover, it must be understood that children born after marriage, no matter how soon, are presumed to be legitimate. Even if the woman be pregnant by an other man and is so far advanced in pregnancy at the time of her marriage that her condition must have been known to her husband, the law deems this a recognition of paternity on the part of the husband, and, therefore, of the legitimacy of the child. As a result of these legal presumptions, it is possible, as Taylor points out, for a child to be conceived before marriage and born after the death of the father or mother (as by Cesarean section) and yet be legitimate although neither conceived nor born in wedlock.

By the common law all children born out of lawful wedlock, whether the fruitful coitus be adulterous or illicit, are styled bastards. While the common law does not recognize such legitimization, the civil law provides that subsequent marriage of the parents renders the issue legitimate. This law has been enacted in California, Idaho, Illinois, Iowa, Maine, Michigan, Minnesota, Montana, Nevada, New Mexico, North Dakota, Oregon, Pennsylvania, South Dakota, and Washington. In addition to the marriage of the parents the father must acknowledge or recognize the child as his in Alabama, Arizona, Arkansas, Colorado, Georgia, Idaho, Illinois, Indiana, Kentucky, Maryland, Massachusetts, Mississippi, Missouri, Nebraska, Texas, Vermont, Virginia, West Virginia, Wisconsin, and Wyoming. In Connecticut, Louisiana and New Hampshire both parents must acknowledge, but in Louisiana the acknowledgment is made either by an authentic act before marriage or by the contract of marriage, and an exception is made of those children born of an incestuous or adulterous connection.[1]

As we have already seen, the normal period of gestation is taken as 280 days from the date of the last menstrual period or 272 days from the date of last intercourse. The laws of different countries vary as to the time which gestation may continue and the child be pronounced legitimate. However, in England and America there is no period fixed by law, within which or beyond which a child, if born in wedlock, will be presumed to be illegitimate. Each case must be decided on its own merits, as the courts may take circumstances into consideration which may prove illegitimacy, while medical facts may support legitimacy. As we have previously mentioned legitimacy has been established in American courts after pregnancies of 313 and 317 days, while a recent case in England has allowed legitimacy after the lapse of 331 days. In suits of contested legitimacy the general practice consists in establishing possibility of access on the part of the husband; if this is proved, the medical question arises whether the term of gestation falls within the limits assigned by the most authentic medical experience.

The law demands that non-access of the husband must be proved to support an allegation of illegitimacy, and, as a corollary, it is presumed that a pregnancy, which could be caused if the husband had access, is actually so caused unless disproven by very substantial facts. As to absence from the country within such a period as would rule out the possibility of the husband being the father, non-access is easily proven. Access, and therefore possible coitus, may be presumed to have occurred on the last day of an opportunity for it, if such presumption could harmonize with the date of delivery; yet the court, if it attacks legitimacy will not hear argument to support a contention that the ovum was not impregnated on the first day of access. Again, a child born within a competent time after access, that is after the last day of life of the husband, or after the last day before the spouses were divorced, is *prima facie* legitimate; and the competent time may be made, in an attack on legitimacy, to begin at an early date by proving non-access or incapacity for a certain period before death or divorce. In the case of non-access before death, the character of the disease of which the husband died is an important consideration. The competent time is the subject of expert evidence in this country.[2]

While the question of legitimacy, as it relates to paternity, has to do with the access of the husband and his capability of procreation as previously discussed, not infrequently the point is raised as to the possibility of the woman being the mother of a child in question. From our previous discussion under the subject of pregnancy, it is obvious that there is no legal age for child-bearing, each woman being more or less of a law unto herself. Thus, girls of 8 and 9 years have given birth to children, while women in the seventies have, also, become pregnant, although the usual span of child-bearing life is from the age of puberty, about 14 or 15, to the menopause, 40–50 years.

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[1] See Dorland, "Legitimacy" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, I, 947.

[2] See Goldwater, "Birth and Legitimacy" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, I, 971.

Supposititious Children.—Another point in connection with legitimacy arises when a woman feigns pregnancy and actual delivery, representing the child of another person as her own offspring. Such cases are usually practiced on account of the possibility of inheritance or of blackmail. The woman may substitute the living child of another woman for a dead one that she actually bore herself, may substitute a male for a female child of her own, or may never have given birth to a child, as was the case of the famous Dolly Matters in Illinois. In such cases it is imperative that the woman claiming to have given birth to a child be thoroughly examined by the physician. It should never be assumed that she has actually undergone delivery from statements made to the physician or from the mere presence of a child in bed with her. As to the child, the physician must satisfy himself that the child presents the appearance of a new-born child and is in every way consistent with birth at the time reported. It is not always an easy matter for the woman, who is practicing such a fraud, to obtain a child that will correspond to one born at the time stated. Thus, a child of one month's postnatal development would not be accepted as the child of a woman whose physical condition indicates delivery within a week. Further, if there has been no birth as far as the woman in the case is concerned, the physician should have no trouble in detecting the fraud, but this can be done only by examination and should never be neglected. It is undoubtedly true that such cases of child substitution and presentation of supposititious children can occur only with the collusion of others and much cunning and duplicity. It is not the duty of the physician to unravel the details of these cases, but he must be in a position to state that the circumstances do or do not warrant the assumption that the woman has given birth to this particular child. The points involved would be the presence of symptoms and signs of an actual pregnancy, signs of delivery, age of the child, and the physical condition of the woman.

PATERNITY AND AFFILIATION

"The question of paternity may arise not only in those cases of birth of a child at some time before the normal duration of pregnancy, but also in cases of posthumous birth occurring over nine calendar months subsequent to the paternal death; in cases of supposititious children advanced as legitimate heirs to an estate; and in cases of bastardy with an attempt at blackmail." At the present time it is hardly possible for a woman to remarry, after the death of her husband, at such a period as would permit the birth of a child within nine months of her remarriage, as the customs of society hardly countenance such practice. If, indeed, a child was so born and might be conceivably the child of either the dead or the living husband, then the fact that it was born during the marriage of the second husband would immediately establish the presumption that the child was his, unless he was in a position to prove non-access and, therefore, no coitus. While such cases of doubted parentage of posthumous children might arise, yet such a situation is extremely unlikely. The law does not pretend to decide who was the father, if the child was born in wedlock, and yet from the circumstances of the case it might be the child either of the husband or another, with whom the wife had adulterous relations.

Such questions of disputed paternity, where the period of gestation does not more or less solve the question, may be determined only by the presence or absence of paternal characteristics of face, form, speech, traits and manner. Such points are usually offered by other than medical witnesses, as the family and friends are in better position to offer opinions on these points because they can speak from personal acquaintance with them. As Taylor remarks," It will also be apparent that the affirmative evidence in such cases will be stronger than that which is negative, for it could hardly be inferred that a person was illegitimate because he did not resemble his parent." Parental likeness may be occasionally indicated by color or peculiarities of race, as when a white woman gives birth to a black child, or *vice versa.* The inheritance of certain characteristics as the color of the eyes or the direction of whorl in the occipital hairs are of considerable importance in deciding the question, although the color of the hair is a very unsatisfactory criterion upon which to base a decision of paternity. Personal deformities of the father are not necessarily transmitted from parent to child, yet Taylor cites a case in which a disputed question of affiliation was settled on this basis.

The question of affiliation (the fixing of the paternity of a child upon a certain individual) is dependent upon the same points as mentioned above. Thus, where two men have intercourse with the same woman within short intervals, the accident of likeness is practically the only one that can be used to settle the point of paternity. In cases of affiliation, under the laws of bastardy, the statements of the mother are received, if corroborated, in support of the question of disputed paternity. Of course, where the period of gestation was not consistent with the actual time of alleged coitus, then the question of affiliation could be overthrown. Where the coitus took place at widely separated periods, then medical evidence as to the period of gestation following such coitus might fix the paternity upon one or the other party.

In connection with these questions of paternity or affiliation, it is important to remember the possible influence of maternal impressions. By this we mean that a woman, while she is pregnant, may be so impressed with the characteristics, either physical or mental, of some man other than the legitimate father, that such peculiarities may appear in the offspring, although there has been no sexual relations between the parties. Under such conditions, the appearances of the child might be such as to warrant the conclusion that a certain man was the father, although in reality he may never have had anything to do with the woman. Another peculiar influence, which is often at work in cases of paternity, is that of telegony. This is the influence which a previous husband exerts upon the children of a subsequent one through the same woman. On such a basis the children of a second husband may have many of the characteristics of a former one. It may be readily seen that complications might arise in a case of divorce with later birth of children, who showed the peculiarities of the former husband.

Blood grouping as Applied to Paternity.—It has been firmly established that the inheritance of the iso-agglutinative group-specific substances in human blood follows the mendelian laws. The medicolegal application is based on the fact that an agglutinogen never appears in a child unless it was present in one of the parents, but it does not necessarily follow that the child *must have* the group of one or the other alleged parent. Hence, it appears possible by a study of the groups of the blood of the child, of the mother and of the alleged father to determine whether or not the child is the offspring of the parties to the case. If the child's blood belongs to the correct group for the alleged parents, it may be their offspring, but if the child's group is wrong as concerns the alleged parents, it must have a parent other than one of those claimed. While this method of testing paternity has not as yet been recognized as infallible, yet it may prove of much value in solving such points. However, as Snyder remarks, "As long as any question as to the efficacy of the technic of grouping or the accuracy of the hypothesis of inheritance remains, the use of the medicolegal application must be attended with extreme caution. Two things are necessary before any character may be used in determining parentage. First, one must be able to recognize without question the presence of the dominant factor in any person. Second, one must be absolutely sure of the hereditary behavior of the character. Until the blood groups can fully meet these requirements, they must be applied in medicolegal cases sparingly and cautiously."[1] Unions of groups O and O give offspring of group O only; unions of groups A and O or of groups A and A give offspring of group A or O; unions of groups B and O or of B and B give offspring of groups B and O; while all unions containing a member of group AB and unions of members of Groups A and B may give rise to offspring in any of the groups. It is probable that the study of the blood groups is, in reality, more valuable in establishing nonpaternity than direct paternity. The proof of nonpaternity depends on the possibility of showing that, according to the laws of inheritance of determining factors, the child could not be descendent of both the woman and the man in question. Hooker and Boyd[1] have figured out the mathematical probability of establishing nonpaternity. They believe that the chances, for a man wrongfully implicated, of proving his innocence are about one in seven. If, however, the blood group of the man is known, the chances of being able to prove nonpaternity may be calculated. If the man is in group AB of the Landsteiner system of classification, there will be 1 chance in 2 of getting final proof; if in group A, 1 in 17; in group B, 1 in 7; and in O, 1 in 5.

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[1] "Blood Grouping and Its Practical Applications" Arch. Path. and Lab. Med., 1927, **4**, 234. See, also, Ottenberg, Jour. Immunol., 1921, **6**, 363; Jour. Amer. Med. Assoc., 1921, **77**, 682; Ibid., 1922, **79**, 873; Ibid., 1925, **84**, 1393; Dujarrie, de la Rivière and Kossovitch, Ann. de méd. lég., 1927, **7**, 390; Merkel, Arch. f. Gynak., 1927, **131**, 188; Schiff, Lanut, 1929, **2**, 921; and *Blood Grouping in Relation to Clinical and Legal Medicine*, by L. H. Snyder.

[1] Jour. Immunol., 1929, **16**, 451.

CHAPTER XIII

ABORTION AND INFANTICIDE

Definitions.—From the medical viewpoint abortion is understood to mean the expulsion of the product of conception prior to the sixth month (twenty-sixth week) of gestation, while the expulsion between the sixth and ninth months is called premature labor. However, the law does not recognize any distinction between the periods of this expulsion, designating as abortion the expelling of the ovum, embryo, or fetus at any period of pregnancy before the term of gestation is completed. As a matter of fact the law seldom has to do with questions of expulsion of the fetus after the period of viability (sixth month) as efforts to remove the products of conception are usually made early in the pregnancy before the mother's condition is very noticeable. By *feticide* we mean the destruction of the life of the fetus before it is fully born and has a separate existence from the mother, while *infanticide* refers to the destruction of the newly-born child which has a separate existence from the mother. Although it might be conceivable that abortion and feticide might in any specific case be synonomous terms, yet this is not necessarily so, as a viable child might be born alive and no attempt be made upon its life after birth, in which case criminal abortion would have occurred, but neither feticide nor infanticide. Further, feticide or infanticide does not necessarily imply criminal abortion, as a premature birth may be due to natural causes, and criminal attempt may be made upon the life of the child during or after birth; or again criminal abortion may coexist with either feticide or infanticide.[1]

ABORTION

Natural Abortion.—It is probable that natural or spontaneous abortion is more frequent than is generally supposed. It has been stated that there are as many abortions and premature deliveries as labors at full term, while Hegar estimates that there is one abortion in the first month of pregnancy to every eight or ten full-term births. It is to be recalled that during pregnancy the uterus is subject to a natural periodical excitement corresponding to what would have been the menstrual periods dating from the last cessation, so that, as stated by Taylor, very trivial causes operating at such periods may lead to abortion. Probably the reason why natural abortion is especially common during the first six weeks of pregnancy is because the ovum is very loosely attached to the uterus and is easily separated and expelled. The period of commencing viability is, also, regarded as an especially critical time. "The actual cause of a spontaneous abortion may be traced to the ovum or the mother. Diseases of the embryo or the fetal membranes may predispose to or determine abortion; in medicolegal cases it is important to remember such causes and exclude them if possible. Some women abort more easily than others, and more easily at one time than another. Some abort on the slightest provocation, while others may be subjected to great violence without disturbing the course of gestation. The ease or difficulty with which the ovum is detached or destroyed depends in great measure upon the healthiness of the ovum and uterus; the health and environment of the pregnant woman are, therefore, important factors in such cases. Other things being equal, weakness, irritability, emotional excitement, and general ill-health facilitate abortion; it is, therefore, easy to understand why some women abort more readily than others, why the same woman aborts more readily in one pregnancy than another, and why abortion is so easy to induce in some, so difficult and dangerous in others. As a general rule a healthy ovum adheres with great tenacity to a healthy uterus."[1]

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[1] See "Abortion and Infanticide" by Cameron in *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 1907, **2**, 355.

Therapeutic or Justifiable Abortion.—It is recognized by both the medical and legal professions that, under certain conditions, the induction of an abortion is justifiable for therapeutic reasons to save the life of the mother. The danger must, however, be real, the bare possibility of death not being regarded as sufficient. It is, however, questionable whether the performance of premature birth of the child is justifiable when the question of saving the life of the child is considered, as such an operation is accompanied with much risk to the mother. It must be admitted that abortion is usually more dangerous and more of a shock to the mother than delivery at full term, where conditions are more or less normal, owing to the danger of hemorrhage and septic infection. However, where definite therapeutic reasons obtain, the risk must be taken, as the mother's life is in jeopardy unless interference is undertaken. There can be no question of legality or morality in such a procedure as the means adopted are employed with a definite hope and intent of benefitting the woman and not with any criminal design, the physician being as much justified, under such circumstances, in inducing the abortion as in performing any surgical operation. In general it may be stated that the induction of abortion is justifiable whenever there is such mechanical obstruction, from pelvic deformity or otherwise, that the birth of a viable child is impossible, or whenever the mother is suffering from such serious disease that her life is in peril and can be saved only by interruption of the pregnancy.

It must be pointed out that the law does not explicitly exempt from punishment the physician who performs an abortion or premature delivery upon a woman with the sole purpose of saving her life. However, in this connection it is necessary to distinguish the action of the physician, who, with intent it is true, does what he can to help a woman upon whom an abortion has been begun either by herself or by others, from the situation which arises when a physician performs a therapeutic abortion. It is true that the law, in its practical working, recognizes that abortion may be necessary under certain conditions, in order to save the life of the mother, and that the act must be performed with a distinct felonious intent to constitute the crime of criminal abortion, yet the physician, must, under such circumstances, protect himself from any possibility of legal action. He should not consider the proposition of interrupting the pregnancy without very careful study and thought and should call in the most capable consultants possible to determine with him the advisability of the step. Further, the consent of the woman herself and of the husband should be obtained before any measures are adopted. As the point involved here is that of saving the life of the mother, the physician is justified in his action, provided there is a definite basis for assuming that the continuance of the pregnancy would be detrimental or fatal to the woman. Ecclesiastic law among some sects is a distinct prevention to abortion. Thus, the teaching of the church of Rome is that no scientific procedure proved to be a therapeutic necessity is refused by the Church, but the destruction of the living embryo is condemned by ecclesiastic authority.[1] In emergency, every effort should be made to save the life of the child in order that it may receive the offices of the church.

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[1] Cameron, *Loc. cit.*, p. 364.

Criminal Abortion.—While at common law abortion was not regarded as a punishable offense if done with the mother's consent before the child had quickened, nor was it a felony to take the life of the child at any period of gestation, yet at the present time most of the states have statutes making abortion punishable by imprisonment if brought about with malicious intent or for an unlawful purpose, and, if the woman die from the effects of the abortion, the crime is regarded as murder in many states, although some set the limit at manslaughter. "To render the offender guilty of murder the elements of that offense must occur with the criminal act. In its present definition, murder is a voluntary homicide committed with malice aforethought, and, in the absence of that element, the offense would not be murder."[2]

While the laws of the states differ in the wording of the statutes as to abortion, yet they agree on the general principles involved. Thus, under the majority of the statutes, any person who, with intent to cause or procure an abortion, unlawfully supplies, prescribes for, administers to, or advises and causes to be taken by a woman, whether she be pregnant or not, any poison, drug, noxious substance, or other thing, or unlawfully uses or causes to be used any instrument or any other means whatever with the intent of inducing an abortion, is a principal either in the commission of the abortion or the attempts to commit it. It is in no sense material, from the standpoint of criminality, whether the person, advising the operation or furnishing the material for its consummation, is or is not present at the time of inducing the abortion..

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[1] See "Abortion" by Davis in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, I, 1001.

[2] See Ex parte Vick (Texas), 292 S. W. R. 889.

It will be noted from the above that the intent to induce an abortion is, in many states, really the basis of the crime and not the means employed to bring about the expulsion of the products of conception. While the laws state that administration of any poison or noxious thing is unlawful, yet it is not necessary that the drug used be proven to be a poison or even noxious, as the drug may be perfectly harmless, the intent to produce abortion being the controlling factor. Further, the question of use of an instrument is covered by the words "or other means whatsoever," so that all that is necessary to prove is that some means were adopted that either actually caused an abortion or were intended to cause it. Under such interpretation a finger has been legally deemed an instrument in such cases.[1]

Further, the woman herself, if she attempts to produce abortion upon herself, is guilty of felony, although such cases are rarely brought before the courts. In her case, however, she must be actually pregnant to constitute the crime. If she die in these attempts, she is guilty of suicide. Consent or solicitation on the part of the woman does not lessen the criminality of the one who assists or performs the abortion, although the woman, unless she be under the influence of drugs or unconscious of what was being done, may be regarded as accessory in some jurisdictions, while in others she is not considered an accomplice.[2] In his charge to the jury in the Whitmarsh case, Justice Phillimore says: "If the unfortunate woman caused her own miscarriage, then, so far as she was concerned, it was in law a case of suicide or *felo de se*. If the prisoner were her accomplice in that, if he were present aiding and abetting an illegal operation which caused her death, though he did not actually use the instrument, he was equally responsible for her death. If he were there, or encouraged or assisted her by getting a room, he would be what the law called a principal in the second degree. If he merely urged or counselled, and was not himself present at the illegal operation, he would be what the law called an accessory before the fact, and would still be guilty of murder." In the Wilson case previously cited, the court held that the woman on whom the abortion has been performed is not an accomplice within the rule requiring evidence in corroboration of an accomplice's testimony in order to convict, although such unsupported evidence is usually regarded as unsafe and much distrust attaches to it.

A further point in the law regarding abortion is that it is not necessary, unless the statute of the state expressly provides the contrary, to prove that the woman, upon whom the abortion was attempted, was actually pregnant. Some of the states have regarded the offense as being greater after the child has quickened, although this point is usually not considered in determining the crime of abortion. It must be remembered in this connection that a woman is "quick with child" from the moment of conception, but is "pregnant with a quick child" only when the period of quickening (fetal movements) begins.

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[1] Wilson *v.* State (Okla.) 252 Pac. R. 1106.

[2] See Thompson *v.* United States, 30 App. D. C. 352.

From the above it is obvious that if a woman tries to commit abortion upon herself, or if another attempts it or aids her in doing so, the woman or other party has committed a criminal offense, no matter whether the woman is really pregnant or not, whether the child is living or viable or not, whether the measures employed actually accomplish the result or not, or whether any temporary or permanent injury has been done to the woman by the attempts, as the criminality of the offense lies in the intent to produce abortion. In Illinois, however, to cause an abortion and to attempt to cause an abortion are separate and distinct offenses. Thus in the case of People *v.* Hagenow,[1] the court said: "It is error to permit a medical witness who had attended the deceased, on a trial for murder by criminal abortion, to testify, over objection on behalf of the defendant, as to the day on which the abortion was committed, where the witness bases his testimony solely on a statement of the deceased. Under the laws of Illinois, to cause an abortion and to attempt to cause an abortion are separate and distinct offenses. Where the defendant is charged with murder by abortion, it is error to instruct the jury with respect also to murder by an attempt to commit an abortion."

In cases in which the physician is consulted by one upon whom an abortion has been begun, either by the woman herself or by others, he should either refuse to have anything to do with the case or, if matters are urgent and the woman is in great need of assistance to prevent a possibly fatal hemorrhage, he should immediately call in another physician as counsel and, also, notify the coroner that he has such a case before him, without mentioning the name of the woman, and is about to do what he can to save the life of the woman. In this way he will probably protect himself against a charge of having been responsible for the abortion, although the law demands rather direct proof that he had nothing to do with the inception of the abortion or with advice concerning methods of producing it. If possible he should obtain a statement from the woman to the effect that the affair was started before she consulted him, but he can rarely hope that the woman will reveal the name of the person who was actually responsible for the act. At best such cases are most unsatisfactory from the standpoint of the innocent physician, but occasionally he will be forced into them from pure humanitarian considerations. However, he should remember that, if the woman dies from the effects of the operation, he may run the chance of being charged with murder for his kind offices. In those states where the law of privileged communications is effective, the testimony of a physician, who attends a woman subsequent to the procuring of an abortion, is not admissable, even when he be sent by the prosecuting attorney to make an examination of her.[1] This rule of privilege does not apply to the relation of physician and patient where such relation exists for the purpose of committing criminal abortion. Communications which have been denied privilege are, as stated by Saylor, a request by a woman to a physician to commit an abortion; communications from one physician to another made to secure the aid of the latter in the commission of an abortion; and where a physician is consulted by a seducer as to the means of producing an abortion.[2] However, in the absence of any showing to the contrary, it must be presumed that communications between the physician and patient are for a lawful purpose and are, therefore, privileged. "Aside from the absolutely legal requirements of the case, the physician has a distinct duty to his patient and to the public. He must not violate his patient's confidence, and his effort should be not only to save her life and health, but, if possible, her character."

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[1] People *v.* Hagenow (Ill.), 166 N. E. 65.

Methods of Producing Abortion.—As to the methods of performing a therapeutic abortion we refer to works on obstetrics, as the means adopted for this purpose must be such as are medically and scientifically the most approved.

As to the method of performing criminal abortion it is to be said that these are manifold and vary in different countries. While with the savages direct violence to the woman is usually employed, such as shaking, beating or kicking her until hemorrhage from the uterus takes place, the means used in the more civilized communities are of two types: (1) The use of drugs; and (2) the use of instruments.

The drugs usually used for this purpose are supposed to act either by causing the uterus to contract (ecbolics) or by bringing about more or less irritation to the gastro-intestinal or genito-urinary tracts. Such drugs as the latter are the drastic purgatives and stimulating diuretics which may be classed, also, as emmenagogues from the fact that many of them at least promote the menstrual flow. It is probably true that there is no drug which is an infallible abortifacient in a healthy woman, with the possible exception of ergot. Various diuretic, emetic and purgative drugs have been employed for this purpose, and, even, mineral poisons such as arsenic, mercury and lead, but they rarely accomplish the result without great danger to the woman. The success of any of these drugs will depend largely on the health and individual peculiarities of the woman involved. If she be one who aborts easily, almost anything which causes marked constitutional disturbance or pelvic irritation will produce the result, while with others none of such remedies will prove successful even when given in very dangerous doses. Besides the above types of drugs used for this purpose, there are many others in common use, among them being preparations of rue, pennyroyal, savin, tansy, and chenopodium, but the real value of such remedies is very doubtful.

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[1] See People *v.* Murphy, 101 N. Y. 126.

[2] See Davis, *Loc. cit.*, p. 1003.

The use of instruments to bring about abortion is more successful than are the drugs, but the danger to the woman is much greater, as perforation of the uterus, introduction of infectious material, air embolism, etc. may follow as sequelae. Among such articles we find that the following have been actually employed in various cases: Sounds, knitting needles, crochet needles, hair pins, catheters, wooden skewers, glass rods, umbrella ribs, pieces of whalebone, scissors, etc. Forcible injections of irritating fluid into the vagina or neck of the uterus has been practiced. In India, according to Bedford, abortion is produced by introducing sticks wrapped in cotton smeared with a paste of pounded nutmeg, capsicum seeds, or croton seeds mixed with arsenic, sulphate of copper, and carbonate of potassium. Of course in the use of any of these methods, much danger arises from the local irritation and possible damage to the uterus and other organs. Not infrequently peritonitis arises from the infection introduced through the perforated area.

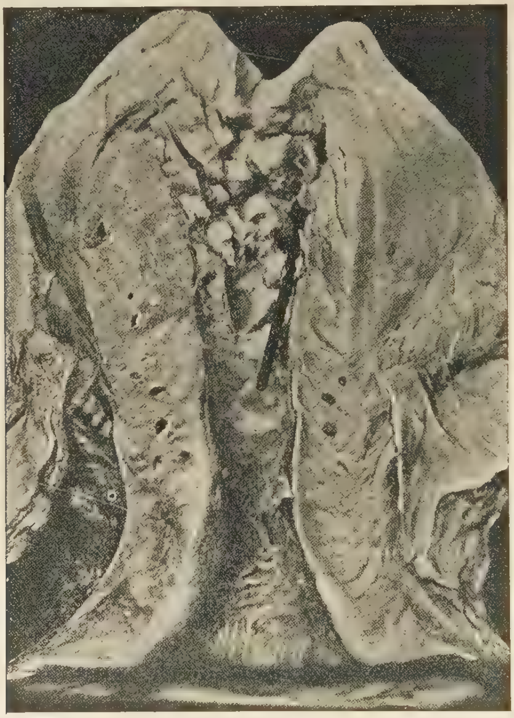

Fig. 25.—Perforation of the posterior wall of the uterus, caused by the introduction into the uterus of a probe-like instrument with the intent to produce abortion. (Hofmann.)

"When the question of morbidity and mortality is considered, it is at once seen that more women die from criminal abortion than from childbirth and its complications. Peritonitis is the most common cause of death, and is responsible for more than half the fatal cases. General septic infection kills about one-fourth. The remainder perish from embolism, pneumonia, or some other incidental infection. Many of the complications which arise in these cases are caused by wounds and injuries to the pelvic organs, perforation of the uterus, tears of the cervix, injection of air or fluid into the blood-vessels, the passing of catheters and sounds into the bladder or the abdominal cavity, or the taking of poisonous drugs may produce lesions of greater or less severity." (Benthin).

Diagnosis of Abortion.—The question as to whether or not an abortion has occurred must be decided upon after an examination of the mother and of the material expelled from the uterus. As a rule, however, it is not possible to make such examinations at a sufficiently early stage to permit of definite conclusions in many of such cases. Of course, in cases of criminal abortion the matter is kept secret as long as possible and is investigated as a rule only when the woman has died from the effects of the operation. As previously stated, under the discussion of signs of delivery, the difficulty of recognizing the condition varies with the remoteness of the time of examination from the actual delivery or abortion. If, as is perhaps more frequently the case, the abortion is performed early in pregnancy there may be little evidence after a few days, so that nothing may be determinable when the examination is actually made. Little opportunity is afforded others than those actually performing the abortion to obtain the discharged material for examination, but occasionally there may be decidual material still in the uterus which may be obtained by curretment for examination, under which conditions a diagnosis will be possible. "Important questions may arise when it is alleged that abortion has been caused by the use of instruments, and death is referred to peritonitis as the result of their employment. In these cases a medical opinion should not be based upon the statements either of the woman or of her friends, but upon some distinct and satisfactory medical proofs that mechanical violence has been done to the womb, its contents, or its appendages. Peritonitis or inflammation of the lining membrane of the abdomen may arise from a variety of causes. If we assign it to a particular cause, and thus implicate another in a felonious charge, we should do this only upon *medical* facts obtained by an examination of the dead body; we should deal with such cases as if we knew nothing of their previous history." (Taylor). The

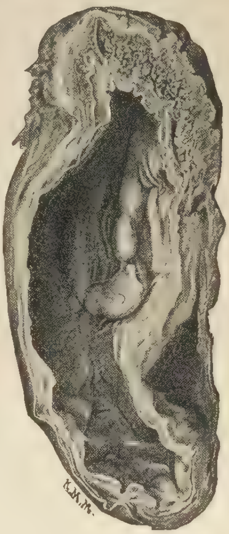
FIG. 26.—Early abortion, showing decidua reflexa and serotina with degenerate embryo × 1. (From Williams "Obstetrics," D. Appleton and Co., Publishers.)

signs of abortion are those previously discussed, but the examiner must not be misled, if nothing is forthcoming from his examination, to make definite statements as to the actual occurrence of an abortion. If there has been careless use of instruments, there may be signs of injury to the parts involved that may point to the probable abortion, but here again there may be nothing incriminating found. If the woman has died and the time of death was not too remote from the time of abortion, a careful post-mortem examination of the uterus and the birth canal may make the diagnosis easy, but if the abortion was early in the pregnancy and the examination of the woman delayed for a few days after this abortion, then little is to be expected from the examination. In some cases abortion cannot be determined definitely after 24 hours, while in others it may be demonstrated after several weeks. Hence, each case must be decided upon its own merits.

INFANTICIDE

Definition.—By infanticide we understand the unlawful destruction of the new-born child. To constitute this crime, the child must be new-born, must be completely without the body of the mother, must be alive when the criminal attack is made, and must die from the effects of this criminal action. This crime is not to be regarded as a specific one, inasmuch as the act is one of wilful murder of a living being, although the specific charge of infanticide usually is made when the child is killed at birth or soon after. Infanticide may occur either through omission or commission, the former covering the neglect to do the usual things necessary to insure the continuance of life of the new-born child, while the latter includes any acts which prevents a new-born child from living or which actually destroys its life. It is immaterial whether the child lives for minutes, hours or days, the charge of infanticide (murder) applying if its life is destroyed after birth. According to the English law, a child is regarded as new-born within 15 days after its birth, so that we would legally speak of infanticide as the destruction of the child at any time within such a period.

As a necessary point in the proof of infanticide, the law requires that definite and satisfactory indications that the child was living when born must be shown. The law assumes that all children are born dead, unless it can be shown that they actually lived after birth, so that the burden of proof in such cases is thrown upon the prosecution to show the actual live birth. As previously mentioned, it is not necessary to show that the child breathed or cried according to the laws of England and America, although in France and Germany evidence of actual respiratory efforts must be produced to constitute a live birth. With us, however, any sign of life, such as wrinkling of the muscles of the forehead, movements of the eye, pulsation in the umbilical cord, etc., are taken as direct indications of life and, therefore, as evidence of a live-born child. It is important that the medical witness bear in mind that his conception of the life of the child is different from that legally established. Medically speaking, life of the embryo begins with the actual fertilization of the ovum and continues until death occurs from some cause, so that the physician would probably be more interested in showing that the child was not born alive rather than in showing that it was so born. However, the law must have some broad basis upon which it can work, in order to enable it to determine when a crime has been committed. Hence, in the legal sense, life of the child does not begin until the child is completely without the body of the mother and is capable of a separate existence. In this connection, it is to be stated that it is not necessary that the umbilical cord be cut, but simply that the child be completely extruded from the body of the mother. The presence of a foot in the vagina, for instance, would not be held as a complete birth in law, and the death of the child under such circumstances would not constitute infanticide if the violence had been administered before complete extrusion of the foot. If the violence to the child occurs during the actual birth, but this violence does not actually cause the death of the child until it is completely born, then the person responsible for such injuries is chargeable with murder just the same as if the violence were actually used after complete birth, while if the child die from the violence before it is completely born, then there is no charge of murder,[1] although it is probable that most jurisdictions would hold that the person responsible for such a death during birth was guilty of an indictable offense, as codified by the criminal law of Canada.[2] It is to be remembered in this connection that the medical practitioner, who in good faith determines that it is necessary to cause the death of the child before or during labor in order to save the life of the mother and resorts to the proper measures, is not guilty of a criminal act.

From the very nature of the case, it is a practical impossibility for the medical witness to state whether or not the injury which caused the death of the child in cases of alleged infanticide was received before or after complete extrusion of the child from the body of the mother, as such cases are usually committed with the object of concealing the delivery or of getting rid of the child in secret so that there are no actual witnesses to the occurrence, unless, of course, the medical man be a party to the crime. For this reason, evidence in such cases does not appear in a direct form but in the guise of assumptions from marks of injury on the body and other signs which would lead the medical witness to state that the child must have been completely born before any violence was exerted. Although the law requires that the child be completely born prior to the use of violence or that the violence exerted before birth does not cause death until after complete birth, yet such a point is difficult of actual proof. However, if it can be shown that actual live birth took place, then the death of the child must have been brought about after complete birth or at least injuries from which did not cause death until after such birth.

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[1] R. *v.* Senior, 1 Mood. C. C. 346.

[2] See Sorel, Ann. de méd. lég., 1928, **8**, 515; and Schmidt, Arch. f. Kriminol., 1928, **83**, 260.

The points to be considered in cases of alleged infanticide have reference, on the one hand, to the mother and, on the other, to the child. As regards the mother the chief point involved is whether or not she has been recently delivered of a child. The special examinations necessary to prove this point have been previously discussed, so that we refer merely to the section on Delivery. If the child be found with the mother, this is probable evidence of the association of the two, but in many cases the child is concealed and often is never found, so that it may not be possible to prove the actual death.

With reference to the child the questions at issue are (1) Was the child a viable one?; (2) Was the child born alive?; (3) If born alive, how long did it live after birth?; (4) What was the cause of death?; and (5) Was the death accidental or criminal?

1. Was the Child a Viable One? We have discussed previously the points involved in the determination of the age of the fetus and its relation to viability, so that we shall simply state here that a fetus less than 7 months of age is not, as a rule, capable of separate existence, or in other words is non-viable, although there are cases of viability at earlier ages recorded. Hence the presumption of the law would be in favor of non-viability in case the fetus bore evidence of less than seven months maturity and infanticide would be difficultly determined in such cases unless there was evidence that an immature fetus has shown some signs of life and had been destroyed by the mother or others.

2. Was the Child Born Alive? It is clear that this question can be answered only when there are no evidences of the child being dead before birth or of incapability of the maintenance of a separate existence, as given by the signs of maceration or putrefaction of the fetus or by signs of non-viability or of monstrous birth. As Taylor remarks: "In these cases it will be first necessary for a medical practitioner to prove that the child under examination has recently died, or, in other words, that there are good grounds for believing it to have been recently living. Hence, if the body is highly putrefied, either from the child having died in the womb some time before birth or from its having been born and its body not discovered until putrefaction had far advanced both internally and externally, the case is beyond the reach of evidence. A medical witness will, in general, be compelled to abandon the investigation because the body can furnish no evidence whatever of life after birth."

While, as has been stated, live birth need not necessarily be associated with signs of respiration such as breathing or crying, yet it is probably true that such signs do furnish the surest proof that live birth has occurred, especially if the medical witness is not present at the time the child was born. Of course, if the physician be present at the time of birth, direct evidence as to live birth is obtainable from the seeing, feeling or hearing of the fetal heart beat or from the pulsation of the cord, even though no signs of respiration are noted. Here, again, the apparent absence of the heart beat is no proof that the child is dead, as the beats may be so feeble that they cannot be distinguished. It is undoubtedly true that a child may live for a certain period after birth without breathing, Bouchut recording a case where the heart beats were audible for 23 hours after birth, although there was no sign of respiration during that time. The destruction of the child during such a period would constitute infanticide just as much as though respiration had been established, yet in the majority of such cases it is almost impossible for a witness to furnish medical data sufficiently satisfactory to permit him to state positively that a live birth has occurred. On the other hand, it must be remembered that absence of signs of respiration is no proof that the child was born dead, as respiration may have been prevented by the mother by placing her hand over the mouth of the child, by being delivered in a bath of water, or by forcing material into the throat of the child and thus preventing access of air.

While respiration is to be taken as only one sign of life and is to be regarded as the most important indication of a live birth, yet the fetal circulation of the blood must also form a definite sign of life and, while it may not be noted before the actual death of the child, it may be indicated by the presence of contusions, ecchymoses, and coagulated blood in areas subjected to violence. In this way, the marks of violence found upon a body of a dead child may give direct evidence that the child was living or very recently dead at the time the injuries were inflicted, as marks of violence on the body of a child dead *in utero* for 24 or 48 hours would not present the characteristics previously described as being indicative of wounds made on a living body. However, the evidence derived from the appearance, extent, and characteristics of marks of violence upon the body is too vague and too uncertain to permit of the conclusion that the child was born alive, although there would be a strong presumption that the violence had been offered after birth, or, in other words, that infanticide had occurred. However, in order to justify any inference as to the live birth of a child under these circumstances, the wounds or injuries should have the well-marked characteristics of wounds made during life (as previously discussed), and "they should be of such a nature that they could not have been produced on the child by an accident when in the womb."

Evidence of Live Birth from the Condition of the Lungs (*Docimasia Pulmonaris*).—Proof of the act of respiration furnishes the strongest evidence that a child has lived at or about the time of birth, but it does not show that the child was born alive. The slightest attempt to breathe after complete birth is, if seen by the witness, absolute proof of a live birth, but it must be remembered that the child may breathe at any time after the rupture of the membranes and, therefore, may breathe in the uterus, in the vagina, or after the head protrudes from the vulva, and yet show no signs of life after being completely born. Under such circumstances the medical witness has no means of distinguishing between respiration which has occurred before complete birth and that taking place thereafter, unless he has direct evidence that the child breathed after complete birth.

It is to be recalled that prior to independent life the lungs have no function and are situated in the back part of the chest, receiving only such blood supply as is necessary for their growth and development. After the establishment of a separate existence and the appearance of respiration, the lungs change in volume, fill up a large portion of the thoracic cavity and all the blood in the body passes through them to be aerated. However, there are not a few cases in which a child is born alive but the lungs remain in their fetal condition, the condition of atelectasis in which the lungs show no signs of having received air by the act of breathing, but may be made to receive air by artificial inflation. Such cases may live for hours or even days, but death sooner or later occurs without any pulmonary signs of life ever being established. Under these conditions, of course, the appearances in the body are the same as in still-born children, so that the signs to be spoken of below do not apply to these cases. It is no doubt, true that fairly strong and regular heart action may continue for a very few minutes after birth without any respiration. Macaggi[1] believes that it is possible for a child under these conditions to receive a certain amount of oxygen by a compensatory exchange of gases with oxygenation of hemoglobin in the stomach, bowel and skin. This worker calls attention, also, to the fact that, when attempts are made to promote breathing by artificial respiration, the infundibula or terminal intralobular bronchioles are found slightly ballooned out, with many hemorrhages caused by the efforts to force air into lungs which possess no alveoli. It is to be said, also, that the air may disappear from the lungs after death.

Generally there is no difference in the condition of the lungs, whether the act of respiration has occurred during birth or after complete birth, but it is highly probable that the process of respiration is rarely so fully established before birth as to give the lungs the feeling of crepitation throughout their area, so that such a condition would be at least very strong presumption that the process of respiration had continued after birth. In the establishment of the respiration there are certain changes in the lungs that would differentiate them from lungs that had not received air, but whether this respiratory effort took place before or after birth would be difficult to decide unless the inflation was so complete as to justify the conclusion that respiration had continued for some time.

(*a*) *Changes in the Volume of the Lungs.*—Before birth or before the child has breathed, the lungs are found in the back part of the chest, occupying a small portion of the thoracic cavity. The thymus gland will be observed occupying the upper and middle portions of the chest, while the heart is situated in the lower middle sector, the lungs never (unless diseased) covering the heart. The lungs in this fetal condition resemble in appearance and in consistency the liver or the other soft organs of the body. A careful microscopic examination of the fetal lung or of the lungs of a child that has been born without any signs of respiration may reveal masses of reticulum rather than air sacs. After respiration has been established, the lungs more or less completely fill the thoracic cavity and almost completely cover the heart, the completeness of this increase in volume depending, of course, upon the degree of the respiratory actions, as there may be intermediate stages of inflation between that of non-inflation and complete inflation. This stage of complete inflation is not so much a function of the time the child has lived as of the thoroughness with which the respiratory act has been performed. As the lungs become filled with air, the tissues have the feeling of crepitation, which is especially characteristic of such inflated tissue.

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[1] Ann. de méd. lég., 1928, **8**, 32.

(*b*) *Changes in the Color of the Lungs.*—Before respiration the color of the lungs may vary from a reddish-brown to a bluish-red or deep violet, the latter being more evident along the margins. After respiration is once established, the lungs acquire a light-red hue with circumscribed patches of a dark bluish-red tint. This so-called marbling is regarded as quite characteristic of lungs that have been naturally inflated by the process of respiration, as the fetal lung shows no such marbled appearance, although there will be more or less marbling if air be forcibly blown into the lungs owing to the presence of blood in the interalveolar and interacinous vessels. However this artificial inflation does not produce the extensive marbling seen in natural respiration and Glaister asserts that "this cannot be simulated by any artificial method." The real truth of the matter is that lungs artificially inflated resemble those organs in which respiration has been only partially established. "On the right lung, and especially on the edges and concave surface of its upper lobe, the first appearances of respiration may be visible, even when the rest of the lungs retain their fetal condition. Here it is that the highly characteristic developed air-cells are first visible. These, if the lungs are fresh and full of blood, take the form of bright vermillion spots; but if the lungs contain less blood, or are examined some days after death, the spots are of a lighter tint." (Taylor).

(*c*) *Changes in Weight of Lungs.*—It is clear that the absolute weight of the lungs before respiration is less than that after this process has been established. On the basis of this change in weight of the lungs, efforts have been made to determine the point as to whether or not respiration has occurred. Two tests have been advocated, one, the so-called Static Test of Foderé, which is based on the absolute weight of the lungs of the child, and a second, the Test of Ploucquet, which is based on the relation of the weight of the lungs to the weight of the body as a whole. It is to be said that neither of these tests has any real value, the former owing to the fact that the weight of the lungs of different children vary widely just as their general body weight varies, so that on conclusion is warranted from such a determination; the latter because there is no fixed relation between the weight of the lungs and that of the body, although Ploucquet would have us believe that the ratio of the weight of the lungs to that of the body was about 1:70 before respiration and 1:35 after respiration.

Hydrostatic Test.—A third test, originally advocated by Raygar, is based on the fact that the specific gravity of the lungs is greater before respiration than afterwards. Although the lungs become absolutely heavier after respiration than they are before this process is established, this is due to the presence of the large amount of blood poured into them at this time. The air received by the lungs in the process of respiration so increases their volume as to more than counterbalance the increased weight derived from the blood and the specific gravity is apparently diminished, so that inflated lungs float on water. It must be understood that the true specific gravity of the lung tissue is not changed by the air introduced, the diminution in this factor being only apparent on the same principle as that of a balloon filled with air. The specific gravity of the lungs before respiration varies from 1040 to 1056; after respiration it is about 940, so that the fetal lung sinks in water, while the inflated lung floats.

The method of performing this test is as follows: Having ligated the vessels, remove the lungs with the bronchi from the chest and place them in a deep vessel of water at about 15° C. Some workers advise the removal of the heart and thymus with the lungs, but this does not seem necessary or even advisable, as we are testing simply the buoyancy of the lungs and not their ability to hold up the added weight of the other organs. The lungs, when placed on the water, will either float or sink. If the lungs float, note whether they float high above the surface or at or below the water-level. Now separate the right and left lobes and test the buoyancy of each as before. After testing in this way, cut each lung into 15 or 20 pieces and test each piece as described. If all the pieces float, remove them from the water and subject them to firm pressure in a towel and test them again, when it may be found that some of the pieces sink, all sink, or all float. If the air in the lungs is derived from natural respiration, no amount of pressure short of that causing disintegration of the tissues will remove it, while if the buoyancy of the tissue be due to the presence of gases of putrefaction, these will be forced out by the pressure and the pieces will sink. If the lungs *en masse* float, if each lung floats separately and each piece of the divided lungs float, the evidence is fairly conclusive that the child has respired freely. If it be observed that part of the right lung floats, while the entire left lung sinks, or that portions of each lung may float or sink, one is justified in stating that the child has breathed, although respiration was not fully established. If, however, the lungs sink when placed on water, each lung sinks separately and the various pieces of tissue also sink, then the point is established that the child has not breathed at all.

Depending on the completeness with which the lungs float, especially after pressure has been exerted to expel the air, this hydrostatic test shows whether or not a child has breathed, but it does not determine whether the child was born living or dead. It must be stated, however, that the lungs of children that have breathed, although very imperfectly, may sink in water owing to atelectasis (fetal condition of the lungs) or to some pathological condition and that a child may survive birth for some time when no part of its lungs has apparently received air;[1] while the lungs of children that have not breathed may float on water due to the presence of air from artificial inflation or to the presence of gases of putrefaction. In these latter conditions, however, the air may be forced out of the lungs by firm pressure, just as it may from lungs in which respiration has been very imperfectly established, so that the tissue will sink when again placed in water. As Taylor remarks: "With regard to the inference derivable from the use of this test, it should be observed that the floating of the lungs in water is not, as it is often incorrectly represented to be, a proof that a child was *born alive;* nor is the fact of their sinking in water any proof that a child was *born dead*. The floating, under the limitations to be described, proves only that a child has breathed; the sinking, either that it has *not breathed* or breathed but imperfectly."

As regards the value of the examination of the lungs as evidence of live birth, it is probable that no single one of the tests is to be regarded as conclusive, but taken together they do form very strong presumptive evidence along this line. Olbrycht[2] believes that the microscopic examination of the lungs affords very valuable evidence, even surpassing that given by the hydrostatic test, and if properly performed so that the condition in different parts of both lungs is determined, affords the best means of demonstrating that respiration has occurred. Casper[3] gives the following conclusions as to the probative value of the *Docimasia pulmonaris:* "The medical jurist is perfectly justified, and may assume with a clear conscience and perfect unconcern as to the results of his opinion, that a child has certainly lived during and after its birth 1. When the diaphragm stands between the fifth and sixth ribs; 2. When the lungs more or less completely occupy the thorax, or at least do not require to be sought for by artificial separation of the walls when cut through; 3. When the ground color of the lung is broken by insular markings; 4. When the lungs are found by careful experiment to be capable of floating; 5. When a bloody froth flows from the cut surfaces of the lung upon slight pressure."

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[1] See Davis, "Infanticide" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, I, 1016.

[2] Deutsche Ztschr. f. d. ges. gerichtl. Med., 1927, **9**, 529.

[3] *Forensic Medicine*, New Sydenham Society Edition, 1864, **3**, 89. See, also, Glaister, *Medical Jurisprudence and Toxicology*, 4th ed. 1921, p. 477.

Evidences of Live Birth from Changes in the Umbilical Cord.—Shortly after the cord is ligated and cut, that portion remaining undergoes certain changes if the child has been born alive or has survived its birth for a period of from twelve to twenty-four hours. It becomes dull in color, slowly dries, shrivels, and separates in from three to five or more days. Mummification or dry gangrene of the cord is not regarded by itself as a proof of extra-uterine life. However, the formation of a line of demarcation, due to capillary congestion, between the living and dead portion of the cord is a sign of vital reaction and, therefore, of live birth of the child. The condition of the cord affords almost irrefragable proof of extra-uterine life, but the time required for such change is, in many cases at least, too long to permit of their recognition, as most cases of infanticide arise shortly after birth. If, however, the child lives for some hours after birth, the physician may obtain invaluable evidence from an examination of the cord.

Evidence of Live Birth from Changes in the Heart and Fetal Vessels (Docimasia Circulationis).—At birth or at the establishment of respiration, the fetal circulation is generally changed to that characteristic of the living child. In other words, it is found that the communication between the auricles of the heart (the foramen ovale), the ductus arteriosus and the ductus venosus become obliterated, but such changes rarely occur before the 8th to 10th day after birth. These structures are all pervious in the new-born child, but gradually become obliterated after a variable period, the umbilical vessels being the first to show the change. The closure of the outer parts peculiar to the fetal circulation is a slow process and sometimes is not completed for years after birth. On the other hand, these parts may become closed and contracted *before birth* and, hence, be found closed in a child born dead, although such a condition must be considered rare. For these reasons the study of the circulatory changes may be considered as more or less useless from the medicolegal point of view. "It either proves nothing or it may lead to an error."

Evidence of Live Birth from the State of the Stomach and Intestines.—Although Tardieu taught that the presence of frothy air-bubbles in the glairy gastric contents indicated live birth for at least a few minutes, yet this can be hardly taken as actual evidence as this same frothy condition could be produced by artificial inflation of the lungs. It has been established that no air is found in the stomach and intestines of the unborn fetus or of the stillborn child. However, in the majority of cases, air probably enters the stomach of the child with the first attempt to breathe and, as breathing proceeds, the air finds its way into the intestines. On the basis of this fact, Breslau advocated a hydrostatic test of the stomach and bowels as an indicator of live birth, the stomach alone floating in case respiration has been only imperfectly established, while the lower the portion of the bowel which floats in water, the greater is the probability that respiration has been fully established. This test has a certain corroborative value, although it is open to the same objections applicable to the lung test, namely that air may find its way into the stomach of dead-born children and, also, that the stomach and intestines of a child may not float on water even though the child has lived and breathed after birth. Where putrefaction of the body is well marked, the results of this test are inferior to those of the lung test owing to the fact that the gases of putrefaction are formed more rapidly in the stomach and intestines than in the lungs and, in consequence the organs will float even though respiration has not been established.

Important evidence as to live birth may sometimes be afforded by an examination of the gastric contents. According to the findings of Robinson, the substances naturally existing in the stomach of a fetus before birth are of an albuminous and mucous nature, while gastric juice is not secreted until after the establishment of respiration. However, in the course of the birth of the child the power of swallowing may be exerted either before or after respiration, so that such fluids as meconium, urine, liquor amnii, blood, etc. may find their way into the stomach. The presence of these fluids would not prove the live birth of the child, but would indicate the existence of vital actions at or about the time of birth. If one finds in the stomach, however, foreign matters, such as water into which the child may have fallen after birth, or starchy materials or milk together with epithelial cells or scales derived from the mouth or throat, almost conclusive evidence is afforded that the child must have been born alive, as it is highly improbable that such material could obtain entrance into the stomach without some attempt at feeding or if the child was born dead.

Other tests of live birth, such as the presence of air in the tympanic cavity as pointed out by Wreden or the uric acid infarction of the kidney, have been advocated, but none of them have any great medicolegal value. Indeed, it is probable that the hydrostatic tests of the lungs, stomach and intestines, and the detection of foreign matters in the stomach are the only ones upon which any reliance may be placed. The status of this question of live birth has been well summarized by Taylor when he says: "The slightest consideration will show that the various indications of live birth above described are weak and of purely accidental occurrence. If a child is destroyed either during birth, or within a few minutes afterwards, there will be no medical evidence to indicate the period at which its destruction took place: the external and internal appearances presented by the body will be the same in the two cases. It is most probable that, in the greater number of instances of child-murder, a child is actually destroyed either during birth or immediately afterwards; and, therefore, the characters above described can rarely be available in practice. If any exception is made, it is with respect to the nature, situation, and extent of marks of violence; but the presence of these depends on mere accident. Hence, then, we come to the conclusion that, although medical evidence can generally show, from the state of the lungs, that a child has really lived, it can rarely be in a condition to prove, in a case of infanticide, that its life had certainly continued after its entire birth. We could only venture upon this inference when the signs of breathing were full and complete, or when some article of food was found in the stomach."

3. How Long Did the Child Live after Birth? It is a rather difficult matter for a medical witness to state how long a child has lived, as there are no certain means for determining the point. In arriving at his conclusions, one must consider both the external appearances and the internal conditions noted.

The *external* appearances of the child have little significance in determining the point at issue, although some general idea may be gained from their observance. If the body of the child be covered with blood and the discharges incident to birth, this would indicate only that the child had not been bathed and would offer no direct evidence as to the period elapsing since birth unless such material had dried upon the body, when it could be asserted that some minutes had certainly elapsed. Nothing of value would be forthcoming from the fact that there was no evidence of such discharges upon the body, as the child may have been placed in water directly after its birth. The presence of vernix caseosa might give more reliable evidence, especially when found in the axilla, groins, and folds of the neck, as this material may remain for a day or so in many children, although it must be remembered that some children are born with little or no vernix caseosa upon their body. Further, the color of the skin may change in tone in a more or less regular way, but again little is to be determined as to the time the child has lived. Usually the skin of the new-born child has a dark red color, but changes within an hour or two to a lighter red and remains of this shade for a day or two. After this time it may become of a brownish-red tint, which may last for three or four days, or may become true yellow from jaundice. In about seven or eight days the skin acquires the normal reddish-white color, which it retains. With these changes in color, one may observe desquamation of the epidermis but this does not occur at any special period. The presence of changes in the umbilical cord may offer some direct evidence as to actual life after birth, but it is to be said that the time when the cord separates varies in different children, so that it is difficult to fix the time of death on this basis, although one may be justified in stating that death may have occurred soon after birth, or, from certain changes, within a day or two after birth.

The evidence offered by *internal* examination of the body of the child is somewhat more reliable than than obtainable from external appearances. The general appearance of the lungs may denote something as to the length of time from birth to death, although the changes are more dependent on the completeness of the respiratory process than of length of life. Atelectasis is usually presumptive of short life, although it must be remembered that quite extensive atelectasis may obtain in a child that has lived for some days. The presence of air in the stomach and in the lower portions of the intestines offers fairly reliable evidence as to the time the child has lived, as the lower portions of the bowel do not receive air until respiration has been fairly well established. If artificial inflation and putrefaction can be excluded, it is safe to conclude that the child did not die immediately after birth, providing air is found in the lower bowel, although as to the exact length of life nothing can be definitely stated.

4. What Was the Cause of Death? It is evident that a child may die either before birth, during birth, or after complete birth, in which cases death may be due to natural or violent causes. Further, it is possible that the violent causes of death may have been accidental or criminal in character. From the medicolegal point of view it is only the deaths from violent causes with actual criminal intent or those in which there has been culpable neglect that can be associated with infanticide. However, as there are many deaths of new-born children from natural causes, the law assumes that the death of the child was due to some natural cause or to accident, until it is proven that it was actually brought about by intentional violence or neglect. It is rare that a charge of infanticide is raised unless there are some indications which point to a possible violent cause of death.

"Many children die before performing the act of respiration, and thus a large number come into the world dead or stillborn. The proportion of stillborn among legitimate children, as it is derived from statistical tables extending over a series of years, and embracing not fewer than eight millions of births, varies from one in eighteen to one in twenty of all births. In immature and illegitimate children, forming the greater number of those which give rise to charges of child-murder, the proportionate mortality is much greater—probably about one in eight or ten. Stillbirths are much more frequent in first than in after-pregnancies; and children are much more frequently born dead among primiparous than among pluriparous women. Males are more often stillborn than females." (Taylor).

There are undoubtedly many deaths of children, in which medical evidence is unable to establish violence as the cause of death, and yet the child may have been intentionally destroyed by exposure to cold, by neglect, or by deliberate prevention of respiration. For this reason, it is necessary for the medical examiner to sift all the evidence he can obtain, before deciding as to the exact cause of death. Further, one must consider not only the cause of death, but, also, the manner in which death has been brought about. Even though there may be marks of violence upon the body, the examiner must not assume that these indicate infanticide, as such marks may have been due to accident before, during, or after birth. It is quite clear that injuries may be produced intentionally or accidentally upon a child in utero, so that death may result from such causes. Blows upon the abdomen, great pressure upon the abdomen, falls from a height, etc., may cause intro-uterine death from fracture of the cranial vault,[1] rupture of meningeal vessels, rupture of internal organs, or multiple fractures of the bones of either extremity. This possibility of such intra-uterine deaths must be borne in mind in order that one may not fall into error in making his decisions as to possible infanticide.

A. Death from Natural Causes.—If it can be shown that death resulted from natural causes or accident, it matters little whether the cause was operative before, during, or after birth, as it is only where a charge of infanticide can be maintained that the death must be shown to have occurred after complete birth.

(*a*) *Causes Operative during Delivery.*—1. *Debility.*—A child, which has been living up to the time of birth, may die from debility during a long tedious labor or may be born either prematurely or at term and not survive its birth for more than a few hours owing to a natural weakness of the system. This type of death is especially observed in immature children, the more immature the child the less the chance of live-birth or the continuance of life after birth. The child may not have sufficient strength to start the respiratory process, and, even if this be inaugurated by the efforts of the physician, the child may breathe only feebly for a short time and then die.

2. *Protracted Labor.*—Protracted labors are among the commonest causes of death of the child during delivery. The greatest danger in such cases is injury to the head and compression of the umbilical cord. Each uterine contraction affects the placental circulation, or the "placental respiration" as it has been called, the stronger and more prolonged the contractions the more prone is the placental circulation to receive an insufficient supply of areated blood and the child may die from asphyxia just as readily as if the respiration were arrested after birth; or the placenta may be partially or even completely separated from the uterus by the strong uterine contractions and, in consequence, the child will die from asphyxia. So, also, one may find that a child, whose head has been born but is held in the outlet by the size of the shoulders, may die from the pressure exerted on the chest by spasmodic contractions of the uterus or by the unyielding nature of the vagina. If the child had breathed and was born dead, the signs of suffocation will be present. If the labor is prolonged and difficult, especially if there be deformity of the pelvis, or if the child be unduly large as related to the size of the pelvis, the head tends to become moulded, after the discharge of the fluids, into the shape characteristic of the presentation and position of the child. Under such circumstances the pressure upon the scalp may cause so much interference with the circulation that swelling of the compressed portion and accumulation of serous material under the scalp may occur,

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[1] See Heidler, Ztschr. f. Geburtsh. u. Gynäk., 1927, **91**, 235.

constituting the so-called *caput succedaneum;* or the serum may be mixed with blood or pure blood may be found under the scalp, forming a tumor like mass known as a *cephalhematoma.* In such cases the head may be deformed by the pressure and the cerebral vessels may be found congested or there may be extravasations beneath the meninges. Even in normal labors, cerebral hemorrhage may arise in the new born from traumatic injury to the blood vessels during the period of molding the head, and, according to Davis, may be caused by intra-uterine or toxemia on the part of the mother. If the pelvis is markedly deformed, the pressure of the uterine contractions, forcing the head down into the pelvis through which it cannot pass, may result in death of the child. It is, of course, in these cases either of deformed or small pelves that Cesarian section is demanded, as otherwise the child cannot be born.

3. *Compression of the Cord.*—It is stated that more than 50 per cent. of the children, in which the cord is compressed, prolapsed, or twisted in coils about the neck, are born as a result of the interference with the placental circulation. The child is really asphyxiated, although respiration has not been established. When a child is born in a foot or breech presentation, the cord may be so strongly compressed that death results. The same thing may be noted in version or forceps cases and in those cases where the coiling of the cord about the neck may so shorten it that the tension is greatly increased by the movements of the child or by the efforts of labor. The child may die from compression of the cord during birth or from tension on the cord after birth. Thus, Davis[1] reports a case where the child was born alive and was heard to cry, but was strangled by the mother when she moved her body away from the child after delivery, thus tightening the cord which was coiled about the child's neck. It should be mentioned that death due to compression of the cord before respiration is established is probably due to asphyxia from an insufficient supply of oxygenated blood, while, if the child has breathed, death is due to strangulation.

4. *Caul Births.*—The delivery of a child with a caul (portions or all of the fetal membranes) around its head is not an especially infrequent occurrence. If the membranes should be carried forward over the head and face, the act of respiration is mechanically prevented and, if assistance is not at hand, the child will soon die. There is little danger from such cases in the ordinary run of obstetric practice, where a physician will at once remove the obstruction, but in cases in which infanticide may be suspected, where the woman may have given birth to the child in secret and no one was near to aid her and she was so overcome by the birth as to be incapable of doing anything for the child, or she made no attempt to aid the child, death will inevitably occur. It is possible in such cases that when the examiner makes his investigation the cause of the interference with respiration may not be found, so that he will probably

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[1] Brit. Med. Jour., 1882, 2, 1069.

report that the child was born dead. Such deaths from prevention of respiration owing to the presence of a caul are accidental and can not ordinarily have anything to do with infanticide, but if no attempt to remove the caul were made by the mother, if she was able to do anything, or if associates simply allowed the caul to remain, then infanticide by omission would be chargeable.

(*b*) *Hemorrhage.*—In children in which the blood shows imperfect coagulability, hemorrhage may occur from the stomach, genitals, rectum, cord, or other organs and may prove fatal in the new-born. However, the most common site of such hemorrhage is from a ruptured, torn, or cut umbilical cord, although sudden separation of the placenta may lead to death from the interruption of the circulation through the umbilical vessels. "The cord may not have been tied after being cut or torn, or it may have been improperly tied, or the ligature may have slipped or been removed purposely, or the ligature may have been stretched or the cord shrunk. The sooner the cord is cut after birth and the nearer to the abdomen, the greater will be the probability of hemorrhage. A cord that is cut with a sharp knife is more likely to bleed than one cut with a dull knife or scissors, or one that has been torn or ruptured." It has been stated that fatal hemorrhage is not likely to occur if the respiration has been established, but there are some cases on record, which indicate that such a statement is erroneous; although the probability of hemorrhage is undoubtedly greater if respiration is absent, weak, or arrested from any cause. Hemorrhage from the cord takes place at various periods after birth and may prove fatal several days after birth, even though the cord has separated by the natural processes. Further, the cord may be torn during labor by the contractions of the uterus and abdominal muscles and the use of forceps may cause fatal hemorrhage from the cord. However, it must be remembered that the division of the cord, either by rupture or cutting, is not necessarily fatal to a healthy child.

There is no doubt that the cord may be ruptured and torn during precipitate births while the woman is sitting or standing, owing to the sudden jerk or strain put on the cord by the weight of the falling child. Moreover, rupture of the cord has been observed when the woman is lying in bed in the usual position and when traumatism and external manipulations could be excluded, as reported by Maygrier. It has been shown by Pfannkuch that, if a sudden jerk be given to the cord, a weight of 500–700 grams will break it, but that a gradual load of 2000–3000 grams may be necessary before rupture occurs, while Spaeth finds that a fresh cord will sustain a weight of eleven pounds (5000 grams).

From the medicolegal point of view, it may be important for the examiner to decide whether the cord has been cut or torn or both cut and torn. This is not always a simple matter to decide, as much will depend upon whether the cutting was done with a sharp or a dull instrument. In a case reported by Gioia the cord was torn during a forceps delivery, the edges being smooth and indistinguishable from those produced by cutting with a knife. The edges of the cord should be submitted to microscopic examination to aid in the differentiation.

Death from hemorrhage is usually recognized by the blanched appearance of the body and the lack of blood in the internal organs of the child. If there should be found severe wounds on the body from which blood has flowed, it must be remembered that the death from hemorrhage may have arisen from the wounds. Moreover, in deciding as to the possibility of death from hemorrhage, it is wise for the examiner to determine whether the cord was cut or torn shortly after birth or was accidentally severed subsequently, as the following case will show: The body of a new-born child was taken from a river in which it had probably been floating for a couple of weeks. The placenta and cord were attached to the body, but in removing it from the water the cord was torn through and the placenta carried away by the stream. The examiner, seeing the cord ruptured and observing no marks of violence on the body, concluded that the cord had been torn by the woman at birth and that the child had died from hemorrhage, but his opinion was disproved by the evidence of other witnesses.[1]

(*c*) *Congenital Malformations.*—It is clear that there may be some defect or deficiency of some vital organ, or there may be some interference with respiration, which would account for the death of the child during or after birth. Thus malformation of blood vessels, absence of any vital organ, malformations of the pharynx, esophagus, stomach, or other organs, spasm of the larynx or fixation of the epiglottis preventing respiration, enlarged thyroid causing suffocation, imperforate duodenum, anus or urethra, etc., may all account for death. Further, monsters may show various types of malformation or they may be so feeble that death soon results.

(*d*) *Congenital Disease.*—A child may be born with such a degree of congenital disease that it is incapable of living for any length of time, or the pathological condition may result in death in utero. Many of these conditions are readily recognizable at post-mortem examination, but there are some obscure affections, especially of the nervous system, that may leave few definite changes in the body, so that the exact cause of death may be in doubt. Certain diseases of the mother, such as syphilis, cancer and tuberculosis, may not result in death of the child for some time after birth, but many such cases of death at birth are observed. The child itself may have certain diseases, especially of the lungs and circulatory organs, so that death will usually result during or before birth. In cases of sudden death of the new-born, the thymus gland may be at fault, being often found much larger than normal and exerting such an amount of pressure on the pneumogastric and sympathetic nerves as to cause the death.

B. Death from Violent Causes.—In many cases of infanticide the body of the child may bear marks of injury, such as wounds, bruises, fractures, burns, marks of strangulation, etc., which leave little doubt that they were produced with intent to kill. However, there are some forms of infanticide, which may not be associated with marks of violence and yet the death is due to direct intent to kill or to culpable negligence on the part of the mother. Such deaths may be brought about by suffocation of the child at birth, by drowning before breathing has occurred, by failure to tie the umbilical cord, by leaving the child exposed to cold, or by depriving it of food. As we have seen, in order to constitute the crime of infanticide and render the woman or associate criminally responsible, it must be shown that the injuries leading to the death were inflicted on a child actually living after complete birth. If the child died from violence carelessly inflicted during birth or afterwards or from culpable negligence the charge may be one of manslaughter instead of murder. It is interesting in this connection to learn that the courts have ruled that, if the child is destroyed before it is completely born, there is no crime committed. It should be remembered, also, that such cases may lay a medical practitioner open to the charge of malpractice if injury to the child at birth results in death and even convictions for manslaughter have been recorded.

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[1] Devergie, Gallard and Devilliers, Ann. d'hyg. pub., 1873, **40**, 443.

(*a*) *Culpable Negligence.*—It is clear that a child may be born alive and die from neglect to tie the cord properly, or it may be suffocated by the clothing of the mother or by the blood and discharges at the time of birth. In such cases the physician, if present at the time, would most certainly be guilty of negligence and might well be charged with manslaughter if such things occurred. However, it is not with the physician that we are concerned as a rule in these cases, but rather with the mother or her associates. It is hardly to be expected that the mother would be in a position to cut and tie the cord or to look after the child after its birth, but it is presumed that a woman who is about to give birth to a child will see that some assistance is at hand, unless she really wishes or intends to keep the matter secret. It is granted that a woman may be seized with sudden labor pains and that she is not in condition to summon assistance under such conditions, but it is a very difficult matter to decide whether or not the labor was so precipitate as to preclude all possibility of obtaining assistance, if this was really desired. However, it is a very difficult matter to convict a mother on the charge of infanticide under such conditions, even though intent were actually present at the time of birth, as there must be direct evidence that the child was actually born alive and was destroyed by failure to do what was necessary to preserve the life of the child. "Unless wilful malice be made out, the accused cannot be convicted of murder, and unless culpable negligence is proved she cannot be convicted of manslaughter." The law holds, as a rule, that if a woman has failed to take ordinary precautions to save her child, she is guilty of criminal negligence, and it could not be expecting too much of a prospective mother that she should see to it that assistance was at hand about the time of her expected labor. It has been said that precipitate labor is not likely to occur with a primipara, so that the plea of sudden birth would not be regarded as a satisfactory defense, but there are many cases of this sudden onset of labor and rapid birth before assistance can be obtained, so that one is not in a position to refute the possibility of such an occurrence in a primipara. With regard to women who have born children, the law assumes that they should know what should be done about the time of labor and that failure to make proper plans and arrangements might be significant of intent to conceal the birth or allow the child to perish.

Cold and *exposure* may readily destroy the life of a new-born child. Simply allowing the child to remain uncovered or slightly covered after birth, especially if the temperature be cool, may rapidly result in death. In such cases there will probably be no marks of violence on the body and the post-mortem findings are usually negative with the possible exception of cerebral congestion with or without serous effusion into the ventricles. As Taylor remarks: "The evidence in these cases must be purely circumstantial. The medical witness may have to consider how far the situation in which the body was found, the kind of exposure, and the temperature of the air would suffice to account for death from the alleged cause. An inspection of the body should never be omitted on these occasions, because it might turn out that there was some latent cause of natural death which would at once do away with the charge of murder." Here, again, the point of wilful malice or of culpable neglect must be taken into consideration, in deciding as to the question of murder or manslaughter, but such points concern the medical examiner only indirectly.

Starvation of the new-born child will sooner or later result in death, and nothing pointing to the cause of death may be forthcoming from the examination of the body. The evidence in such cases is largely circumstantial, as the medical evidence pointing to starvation is slight. The contents of the stomach should be examined for food residues, as the only appearance likely to be found in such cases is almost complete emptiness of the stomach and bowels. However, this would not be sufficient to prove the point of wilful deprivation of food with criminal intent to destroy the child.

(*b*) *Asphyxia.*—This is one of the commonest forms of death of the new-born child and may be brought about during or after birth and before or after respiration has been established. However, strictly speaking true asphyxia with its post-mortem findings can occur only after breathing has occurred. The cases of death, which occur before any respiratory efforts have been made, should, more properly, be spoken of as being due to prevention of respiration.

1. *Suffocation.*—Many cases of so-called suffocation arise from accidental or even wilful acts at the time of birth. Thus, a child may be prevented from breathing by obstruction of the mouth and nose by the body or clothing of the mother; the child may be placed face down-

wards on a soft pillow or feather bed; the child may be born in a bath of water; the child may lie face downwards in the bloody discharges from the mother; the child may be born with a caul; or the air-passages of the child may be obstructed with mucus, meconium, or blood. There are quite a number of cases reported in which a woman, mistaking her labor pains for a desire to urinate or defecate, has gone to the toilet where the pains have been so strong that rupture of the membranes has occurred followed by precipitate birth. In such births the child may fall into the closet and be prevented from breathing by the closure of the mouth and nostrils by the fluids and solid material. In many of these cases it is a more than difficult matter to determine whether or not the death was really accidental or intentional.

Infanticide by suffocation is frequently observed, such cases often furnishing clear evidence of the wilful destruction of the child. Thus, a child may be closely wrapped in the bed-clothes by the mother; the mouth of the child may be stuffed with feathers, wool, mud, clay, ashes, dough, sand, pieces of sponge, handkerchiefs, etc., as shown by reported cases; the mouth of the child may be covered with a wet cloth or by the hand of the mother; or even tight compression of the body may be employed. In these cases the evidences of asphyxia will be clear if the child has breathed and will be those previously discussed in the chapter on Asphyxia. A careful examination of the mouth and throat may reveal the cause of the obstruction to respiration, the occluding substance often being found therein. Further, the use of violence may be assumed from the irritated or lacerated condition of the mouth and throat. From the legal point of view it matters little whether the occluding substance found its way into the throat by the forcible thrusting of such material into it or by aspiration, as the death was due to intentional obstruction of respiration in either case and intent must be assumed. Evidence of violence inflicted upon the body will excite suspicion in many such cases, but it must be remembered that there are unquestionably some cases of wilful suffocation of the new-born child in which no evidence can be obtained as to the exact method of causing the death.

2. *Strangulation.*—This form of death is usually associated with appearances which indicate criminal intent on the part of some one, but it must be remembered that there are forms of accidental strangulation of the new-born child which can hardly be distinguished from those due to violence. Criminal violence is usually indicated by the degree of injury to the neck, the violence being overdone as a rule in homicidal cases.

The usual means of strangulation in cases of infanticide are those employed with adults, that is by compression of the neck with the hands or with ligatures. In such cases the signs of death are those previously discussed. It must be admitted that there are cases of death of the child from coiling of the umbilical cord about the neck, but these usually occur in utero and the child dies from compression of the cord and arrest of the fetal circulation rather than from true strangulation. In the strict sense strangulation can occur only after respiration has taken place. However, there are cases reported in which the cord is so shortened by the twisting about the neck that the child can not be born until the cord is divided. In such cases the child may breathe as soon as the head is born and be strangled before complete birth occurs. The marks of constriction may appear as broad, shiny, depressed bands circling the neck and there may even be some ecchymotic spots along the lines of constriction. It must be borne in mind that the marks of constriction about the neck can not distinguish positively between accidental and intentional strangulation, except that these may be more distinct and the damage to the neck more marked in the latter case. As Cameron remarks: "It is entirely a question of degree, but it is improbable that the cord could be accidentally tightened during birth so as to produce marks resembling those resulting from criminal violence, while at the same time the child is able to breathe sufficiently to expand the lungs fully with air." In death due to ordinary constriction of the cord or to tightening of the cord after the head is born, the circulation is shut off and death results from this cause with no expansion of the lungs, but the cases reported show that this situation of shortening of the cord may arise after the head has been born and the child has breathed, so that the examination of the lungs would indicate death from strangulation, thus leading the medical examiner into possible error as to the time when the death occurred. "When the mark on the neck is deep, broad, much ecchymosed, and there is extravasation of blood beneath, with injury to the muscles or windpipe, and ruffling or laceration of the skin, it is impossible to attribute these appearances to accidental compression by the navel-string. The lividity produced by it in the cases hitherto observed has been only slight and partial, and unaccompanied by laceration of the skin or injury to deep-seated parts." However, if the cord be intentionally wrapped about the neck and used as a ligature, as it has been in some cases, the injury to the neck may be as great as when some other type of ligature is used, but the cord on examination will reveal signs of stretching such as do not occur in cases of accidental strangulation. If the child has fully breathed, the presence of a deeply ecchymosed or edematous groove on the neck with more or less injury to the skin and muscles is generally regarded as presumptive of intentional strangulation. However, it is hardly possible to determine from external appearances whether the constricting force was applied during life or shortly after death, as the evidences of strangulation would be shown, according to Casper, if the compression were applied within an hour after death. Further, it must be stated that one is not in a position to determine whether the strangulation occurred before or after complete birth of the child, unless there were other evidence than the appearances of the neck and lungs.

3. *Drowning.*—Drowning may be either accidental or intentional. The signs of drowning of a new-born child do not differ from those

in adults providing respiration has been established, but it must be remembered that drowning can not be proven by medical evidence if the child has not breathed. While cases of drowning of the child before respiration has occurred are rare, yet there are cases in which the woman was delivered in a bath and the child forcibly held under water until death occurred, under which circumstances no evidence as to the mode of death would be found on post-mortem examination.

Infanticide by drowning is not very common, as death usually occurs from other causes such as suffocation, strangling, violence, etc., and the body is thrown into the water either to conceal it or to cover up the real manner of death. If a body is found in the water, it must be determined whether or not the child was living when thrown into the water, and whether death was really due to drowning. In this connection it is to be recalled that it is not necessary that the body of the child be submerged in order for drowning to occur, as the simple covering of the mouth and nose with fluid is sufficient to drown a new-born child, the symptoms of asphyxia appearing relatively soon. In making his investigations the examiner should pay special attention to the throat and air-passages, noting whether foreign substances, such as dirt, straw, fecal material, etc., are present in order that he may have some idea as to the possibility of the drowning in a particular place. The lungs will, of course, give direct evidence as to the establishment of respiration.

Whether or not the drowning was accidental or intentional is a question for the jury to decide, but the medical evidence may prove valuable in settling the point. Marks of violence upon the body, or the signs of death from strangling may be strong presumptive evidence in favor of death before immersion, but it must be admitted that much violence may be done to the body while in the water, so that, in order to prove of value, "all marks of violence on the bodies of children that have died by drowning should be such as to have resulted from accidental causes."

C. Wounds.—Wounds are frequently the cause of death of the new-born, and these may, of course, be either accidental or intentional. There are cases reported of death from natural causes in which wounds are found on the body, so that the mere presence of a wound does not necessarily imply infanticide, nor does the presence of an apparently slight wound indicate that death is not due to the damage caused by the instrument making the wound.

Wounds on the new-born may be of the same nature as those found on adults, that is they may be incised, punctured, lacerated, gun-shot, etc., and the same points will apply in determining whether such wounds were made before or after death as have been previously discussed. The points in which the medical witness is most interested are whether the wounds were produced before or after death; whether they were sufficient to cause death; and whether they were accidental or homicidal.

As regards accidental wounds it is to be said that such may be produced when a knife or scissors slip in cutting the cord and incised wounds result; or very severe wounds may be made by the slipping of the forceps during delivery; or fractures of the skull may occur by the striking of the head against hard surfaces in cases of sudden or precipitate birth; or the head may be so twisted that dislocation of the cervical vertebrae may occur. With reference to injuries to the head it must be recalled that marked damage may be done during a protracted labor in cases of deformed or contracted pelves. Although fracture of the bones of the skull does not necessarily take place even when great violence is exerted, yet such injuries do occur from the strong uterine contractions forcing the head against the pelvic bones and even from the strong pressure exerted when the head passes through the external os, or from pressure of the forceps during delivery. Such fractures are, as a rule, slight and ordinarily amount to simple fissures in the bones beginning at the sutures and extending a short distance into the body of the bone, the frontal and especially the parietal bones being the ones usually affected. While fractures of the bones of the skull may occur following precipitate delivery, it is seldom, as Tidy remarks, that such falls are the direct cause of the death of a child. If it dies under such circumstances, hemorrhage from a ruptured or a torn cord, premature separation of the placenta, or cerebral hemorrhage is more likely to have caused the death.

Intentional wounds on the body of a new-born child may appear very trivial but, nevertheless, may produce fatal results. Thus, the brain may be pierced through the fontanelles, the nose or orbit by needles or other small instruments; the spinal cord may, also, be injured in the same manner by introduction of the instrument between the vertebrae; or the heart may be pierced by such instruments as knitting needles and the site of puncture appear very superficial. In the case of fractures of the skull from violence purposely inflicted, the injuries are usually far more severe than those of an accidental nature, as the tendency is to do much more than is necessary to produce death. The fractures are often multiple and the skull may appear as if battered in by the force used. The degree of injury noted, especially if several points of injury are observed, is of great value in permitting a judgment as to homicidal or accidental cause of death.

D. Poisoning.—Death from poisoning of new-born children is rare, although it has been reported occasionally in the literature. Opium in some form, especially as found in soothing-syrups, is perhaps the commonest poison used, yet there are cases of poisoning of the new-born with arsenic, phosphorus, mercury, etc. Tardieu records the murder of two very young children by means of sponges dipped respectively in nitric and hydrochloric acids. In such cases of poisoning it is a very difficult matter to fix the administration of the poison upon the really guilty party.

5. Was the Death Accidental or Criminal? From the previous discussion it will be observed that there are many natural causes of death of the new-born child and that there are, also, many deaths from violence which may be either accidental or intentional. While the determination of this question is a matter for the jury, yet the medical witness is often called upon to state his ideas as to the cause of death, so that he must take into consideration the various factors of each case with which he is confronted before he makes any definite statements one way or another. Each case must be decided upon the direct evidence obtained by the examiner, but circumstantial evidence will, also, weigh heavily in each case. While certain points previously mentioned will tend towards the assumption of infanticide, it must be remembered that it may be possible to show, when the evidence is all in, that the death was more of an accidental than a criminal nature. It is, therefore, not possible to lay down any rule by which one may judge that a certain case is one of infanticide and another an accidental death. Every available point must be considered and even then doubt may exist.

CHAPTER XIV

RAPE AND UNNATURAL SEXUAL OFFENSES

Rape is defined as carnal knowledge of a woman by a man accomplished by force and against her will. By the expression "against her will" it is to be understood that the act is committed without her consent, for it is evident that there is no crime if the woman consent to the act, although it may constitute illicit intercourse or adultery. This consent, however, must be free, voluntary, and conscious and not obtained by fraud, deception, fear, or moral or physical force. The law fixes the capacity of a female to give consent more or less definitely by her age. By the common law of England, a female is incapable of giving consent if under thirteen years of age; if she be between the age of 13 and 16 carnal knowledge is a misdemeanor; while if over 16, her consent, if freely given, relieves the male of any blame. In the United States the age of consent varies more or less. Thus, in some of the southern states (Alabama and Mississippi) it is 10 years; in Louisiana and Texas it is 12; in most of the middle states it is 14; and in some of the eastern states it is 16. The laws of the various states hold that intercourse with a female below the age of consent constitutes rape, charging a felony or a misdemeanor according to the jurisdiction, so that the element of force does not enter into such cases.

The law holds that the handling, touching, or attempting to touch by a male any part of the genital organs or breasts of a female (or in some states feeling the legs) without her consent constitutes an assault, the penalty for which varies in the different states, and is severe in most of them, some states not making much distinction in the sentences given for such assaults and rape. In the earlier statutes and decisions carnal knowledge was understood to mean complete intercourse with emission of semen, but at the present time the courts rule, practically without exception, that the slightest penetration of the female organs by the male organ is sufficient to constitute rape, if made against the will of the woman and under either moral or physical force, or, if the victim be a child under the age of consent, penetration constitutes rape even though no force be used. The degree of penetration is immaterial, vulval penetration with or without injury to the soft parts being regarded as rape just as much as full vaginal penetration with or without rupture of the hymen.

The force used must be sufficient to accomplish the purpose, in many cases being of an extremely brutal nature. The question has not infrequently arisen as to whether a healthy, able-bodied adult woman can be raped by one man. While most authorities agree that such an occurrence is improbable providing the woman has not been rendered unconscious either by a blow or by some stupefying drug or has not been so terrified or mentally affected by the assault that resistance is impossible, yet that such cases do happen is apparently shown by the report of the rape of the young woman F by the man L as given by Casper.[1] However, where the man is very powerful and the woman is young, very old, or physically weak, the possibility of a successful rape would be increased; on the other hand, if a full grown vigorous woman is attacked by a boy or by an aged or feeble man, the woman should be able easily to prevent the rape. In other words, each case must be decided on its own merits, as the woman ordinarily should be able to prevent the penetration by movements of her body, unless she is deprived of her senses by some means. It is important that we recognize here that physical force is not alone necessary to constitute the crime of rape, as moral force, such as may be used by threats against the woman herself or against some member of her family, may be quite as compelling in forcing the woman to submit as the more brutal physical assaults.

"Resistance is the most immediate expression of the act being against the will of the female. This must have been manifested positively by her, or she must have been in a physical or mental condition precluding its expression, to make an act of intercourse with her rape. Absence of resistance as a result of physical incapacity, narcotism, or mental disease is not construed to change the character of an unlawful act of intercourse."[2] The resistance of the woman must be to the limit of her power. In some cases it may appear that she has resisted in the beginning but has voluntarily yielded later owing to the fact that her physical powers have been taxed to the limit. Dread of violence or even fear of death may prevent a woman from offering resistance, but such forced assent does not relieve the assailant of guilt. As Tidy remarks: "If non-resistance on the part of a prosecutrix proceeds merely from the female being overpowered by actual force, or from her inability owing to want of strength to resist any longer, or from the number of persons attacking her rendering resistance dangerous, or at any rate absolutely useless, the crime is complete. And it will not be any excuse that she was first taken with her own consent, if she were afterwards forced against her will; nor will it be a defence that she consented after the fact; nor that she was a common strumpet, or the concubine of the ravisher; for she is still under the protection of the law, and may not be forced."

It is interesting to note that the English law, following the old dictum of Lord Hale pronounced in 1650, presumes that a boy under the age of 14 is incapable of committing a rape, a legal presumption which is certainly at variance with physiological facts and recorded cases. Although it may be true that we have no definitely established cases of a boy under

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[1] Case LIV, *Forensic Medicine*, New Sydenham Society Edition, 1864, **3**, 311.

[2] See "Rape" by Chaddock in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, I, 1033.

14 becoming a father, yet coitus does unquestionably occur at very much earlier ages as many reported cases indicate, so that a rape may be accomplished at an earlier age than 14 as the law holds simple penetration of the female organs as one of the essential factors of this crime. Indeed, Chevers of India cites a case of conviction of a boy only ten years of age for rape on a girl 3 years old.[1] In this country, however, this presumption of law is held to be changed by climatic and other conditions. Thus, in the case of Hillabiddle *v.* State[2] climate was first considered as modifying the age of puberty and liability was placed on the ground of ability to consummate a carnal connection. In the case of Williams *v.* State the presumption of incapability was held to be rebuttable by proof that such a person has arrived at puberty.[3] In other cases it was held that the presumption of physical incapacity can no longer be held to be conclusive[4], while still other rulings hold that physical capacity must be determined by the evidence.[5] These latter rulings are upheld according to Edgar and Johnston[6] by the laws of all the United States, with the exception of North Carolina, Florida, and California, which conform to the English statute.

The fact of consent on the part of the woman is of primary importance in determining the question of rape. Naturally, voluntary consent to intercourse would relieve the man of any guilt beyond the possibility of a charge of adultery or of bastardy. However, in cases of alleged rape, consent is determined largely by the lack of resistance made by the woman, but it must be remembered that the woman may be rendered incapable of resistance as previously mentioned, so that a charge of rape might be substantiated even though no resistance was offered by the woman, providing it could be shown that she was physically incapacitated, was forced to submit by threats or by fear, was mentally incapacitated, or was under the influence of drugs. The crime cannot be regarded as actually consummated, as previously stated, unless the woman resist as much as she could, but a forced assent, obtained through threats of violence or of death to herself or some member of her family, does not excuse the offender, as moral force is just as potent in forcing consent as is physical force. It should be remembered, as Chaddock remarks, that nothing is so likely to cause temporary psychic paralysis in a woman as a violent and unexpected sexual approach.

It has been questioned whether a man can have intercourse with a woman without her knowledge while she is in a state of unconsciousness from natural sleep. If this be possible, a further question arises; namely is the accomplishment of the act tantamount to consent on the part of the woman? It is very unlikely that complete coitus could occur during normal sleep of the woman, unless she was accustomed to intercourse and her sleep was very deep, but the possibility of the offense being perpetrated under such conditions cannot be denied. Many alleged cases of this type of assault have been reported, but in all of them there is a question of more or less doubt of the real truth of the woman's assertions, although a case cited by Taylor would seem to indicate the possibility of intercourse during sleep.—"The respectable wife of an innkeeper, who had children, threw herself on her bed with her clothes on late one evening and fell fast asleep. She was first awakened by finding a man upon her body in the act of withdrawing from her. This man, McEwan, a servant in the house, was given into custody on a charge of rape. In the first instance he did not deny the act, and there was no reason to believe that the prosecutrix was aware of the prisoner's conduct until the crime was completed, and she was awakened in the manner described, apparently by the weight of the prisoner's body. The prisoner was convicted."[1] However, with a virgin, such a case would seem to be impossible as the first act of coitus would almost certainly arouse a woman from any ordinary sleep, although it must be admitted that the circumstances of the case might so facilitate the initiation of the sexual approach that, when the woman was aroused, her resistance would prove of little avail. If unlawful intercourse does occur under these conditions, the charge of rape can be sustained on the ground of lack of consent.

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[1] Quoted by Taylor, *Medical Jurisprudence*, 12th Amer. Ed., 1897, p. 653.

[2] 3 Ohio St. 52.

[3] 14 Ohio St. 222.

[4] See Waggoner *v.* State, 5 Lea, Tenn. 352.

[5] See State *v.* Young, 3 So. Rep., Louisiana, 57.

[6] "Rape" in *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 1907, **2,** 728.

An interesting question arises in this connection as to whether it is rape in cases where a man has intercourse with a woman, while she is asleep or awake, the woman believing the man to be her husband. There are many such cases reported, and it must be admitted that the situation is very favorable for the accomplishment of the act, but does the fact that the intercourse is permitted carry with it the consent of the woman to the fraud perpetrated upon her? Decisions have been rendered upon both sides of the case in the English courts, the dictum that "where consent is obtained by fraud, the act does not amount to rape" being supported or refuted in the different cases.[2] However, the English statutes have now taken cognizance of this inconsistency and have enacted by the 48 and 49 Vict.c.69 the following: "whereas doubts have been entertained whether a man who induces a married woman to permit him to have connection with her by personating her husband, is or is not guilty of rape, it is hereby enacted and declared that every such offender shall be deemed to be guilty of rape." Convictions for rape under the above conditions have been given in New York and Connecticut[3], although in some of the other states intercourse under these circumstances is not regarded as rape, on the ground that when fraud has been the means of accomplishing coitus, the act cannot legally be construed as rape unless it can be shown that there was intention to use force, which the success of the fraud made unnecessary. Such interpretations would seem to be inconsistent, as the man would probably have used force to accomplish his purpose had it become necessary and his deception precluded the sound judgment of the woman.

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[1] See Edinb. Month. Jour., 1862, **2**, 570.

[2] In this connection see R. *v.* Saunders, 8 C. and P., 265; R. *v.* Williams, 8 C. and P., 286; R. *v.* Barrow, L. R., 1 C. C., 156; R. *v.* Young, 14 Cox, 114.

[3] People *v.* Metcalf, 1 Wheel, C. C. 378; State *v.* Shepherd, 7 Conn. 54.

Another type of fraud occasionally practiced on women, especially those of youthful age or of lowered mentality, is that in which medical men represent that certain measures are necessary in the treatment of the case and then resort to sexual intercourse, the female submitting from ignorance as to the nature of the act that is taking place. Thus, in a case in England a physician had carnal knowledge with a girl of 14, who was suffering from suppressed menstruation, he telling her that it was a necessary part of the treatment, and she, from her youth, being ignorant of what was taking place.[1] In another case intercourse was effected by a physician under the pretence of giving an injection.[2] Conviction followed in both these cases. So, also, in a similar case in Indiana conviction for rape has followed.[3] In such cases, however, it is to be said that if the defendant has reason to believe that the woman assented to the act, a prosecution for rape cannot be sustained. To rape, under such circumstances, an intention to use force is essential, but such intention cannot be inferred where there is true belief in consent.

As regards assaults upon women of markedly lowered mentality it is to be said it is a rape to have sexual intercourse with an idiotic, imbecile or insane woman, even though she does not dissent, as she is not regarded as being capable of intelligent submission. However, in cases of mental disease which do not reach the above states, there is no rape if consent be given and no force employed. If, however, there is actual incapacity to consent, and force is used, the offense is rape. It seems to be clear, however, that in any case of alleged rape upon a mentally unsound woman, some evidence must be adducted to disprove assent to the act, and should there be none, a conviction is questionable.

If narcotics or intoxicating drinks be given to the woman, so that she becomes more or less influenced by them and intercourse be had, the male is guilty of rape although no force has been used. As Wharton and Stille[4] remark: "It makes no matter whether the drug was given for the purpose of producing stupefaction, in order that the rape might be effected on the female thus made unconscious, or whether it was administered for the purpose of causing sexual excitement, and thereby leading to a voluntary submission. It is rape in either case, supposing the woman to have been made incapable of resistance, the law being, that the overcoming of chastity, and the destroying of resistance by artificial means, is rape, when the offense is consummated. If the result of the dose be stupefaction, and if, on the woman thus become insensible, carnal intercourse be effected, it is rape, though the intention was merely to excite." Chloral hydrate, opium, chloroform, ether, and other drugs and anesthetics have been employed to stupefy the victim, while aphrodisiacs such as Spanish Fly have been used to excite her, but the nature of the drug used is immaterial, as coitus constitutes rape if the woman be under the influence of the drug. It is to be remembered that the narcotics act slowly and that it is a difficult matter to anesthetize a woman against her will, unless perhaps she be asleep, so that where statements are made that immediate loss of consciousness occurred from the mere holding of a handkerchief against the nose, suspicion should be aroused that the woman is not telling the truth. It is more or less common for women to have delusions of an erotic nature during the administration of an anesthetic, especially of nitrous oxide (laughing gas), so that one need not be surprised if charges of assault are made, when the woman recovers from the anesthetic. Such charges are rather frequent and, while it must be admitted that there are occasional cases of assault under such conditions, yet most of these charges are false and utterly without foundation. To protect himself when administering an anesthetic to a female patient, it should be an invariable practice of the physician or dentist to have a third party in the room to testify as to the facts should such unfounded charges arise. As regards alcoholics it is to be said that they are frequently taken only to the point where the woman loses her sense of control and readily consents to the intercourse, under which circumstances the courts would probably not rule that rape had been committed, although there could be no excuse for the man taking advantage of the woman. However, if the alcoholic be taken to the point of loss of consciousness and coitus occurs, the act is rape as there is no consent under such circumstances.

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[1] R. *v.* Case, 1 Den. Crown Cases, 580.

[2] R. *v.* Stanton, 1 Car. & Kir. 415.

[3] State *v.* Pomeroy, 94 Ind., 96.

[4] *Medical Jurisprudence*, 4th Ed., 1884, **3**, 435.

Testimony.—Under ordinary circumstances it is evident that there are no witnesses to the crime of rape other than the woman and her assailant. For this reason, the law considers the testimony of the victim, the prosecutrix, as offering legal proof of the act of assault. While the law fixes no limit as to the time when a woman may make her complaint against her assailant, yet the sooner she makes the assault known the more likely is the charge to be regarded as based on fact, although a long delay should not prejudice the case if she was still under the control of her assailant and had more or less fear of him. As the woman is a competent witness to the attack, it is not surprising to find that many cases of false accusation of rape are made and that many an innocent man is put in jeopardy by the assertions of a woman, who swears falsely from motives of jealousy or of revenge. Indeed, Amos states that for one real rape tried in the courts there are on the average twelve pretended cases, an assertion which is probably somewhat too strong, although Taylor believes that common experience bears out this statement. Edgar and Johnstone, from a study of 176 cases in which certificates of complete penetration were given in 108 and 44 convictions were secured, believe that the dictum of Amos does not always hold good. It is probably true that most of the false accusations are made by children, who are terrified by their parents or friends into accusing perfectly innocent individuals of having taken indecent liberties with them, but many cases of false charges by adult women are on record. As the evidence of the woman will usually afford *a priori* proof of the assault, the character of the woman may be assailed in rebutting her statements, but it must be remembered that, even though the woman be a common prostitute, if sexual intercourse be had with her against her will and with force, her assailant is guilty of rape. Cross-examination of the woman is, of course, permissable as to the amount of resistance offered by her, as to the location of the attack, as to whether or not she made any outcries, etc., in order to show whether there might have been an element of consent on her part. The charge of rape is, as remarked by Tidy, hard to prove in many cases; but it is still harder, considering the legal definition of rape, to disprove by an accused person, even though he be innocent. And false charges being so common, medical men must be specially careful not to be the dupes of impostors.

Corroborative Testimony.—As the unsupported evidence of the prosecutrix has so often lead to false accusations and even conviction of innocent parties, judges are coming more and more to require some corroboration of the evidence of assault and juries are more loath to convict in cases in which there is no further confirmation than the mere statements of the parents or friends of the alleged victim. The most important corroborative testimony is medical in character, although too often the complaint is not made until so long after the alleged assault that nothing of value will probably come from the medical examination. Of special importance in this connection is the possibility of the medical witness detecting inconsistencies in the statements as to the alleged assault and, in this way, clear-up false accusations of rape.

It is clear that if the medical evidence is to be of any value in determining the points at issue in the case, that is whether or not there has been penetration of the sexual organs of the female by the male organ and whether the coitus occurred against the will of the woman as shown by signs of violence in and about the female organs or upon the body of the victim, such examinations should be made relatively soon after the alleged assault has taken place. It is rare that the woman presents herself for examination until some time has elapsed following the alleged rape, so that such points of evidence, as some writers lay stress upon, as the disordered state of the clothing, the muddy or soiled condition of her garments, and even the presence of spots of blood or semen on the underclothing, may not be capable of determination. In this connection an interesting decision has been rendered[1]. In this case the defendant was convicted of rape of a girl less than 18 years of age. Objection was raised against testimony of a physician based on an examination made about 2 months after the alleged assault. The Supreme Court held that the evidence was admissable notwithstanding the claim of the remoteness, the objection going rather to the weight of the evidence than to its admissability. It tended to establish that the prosecutrix had intercourse with some one, constituting rape at her age, and to that extent to corroborate her statements. Such evidence might be plainly corroborative of the commission of the crime by someone, although it would not establish the defendant's connection with it.

When the physician is called to examine a woman upon whom a rape is said to have been made, he should note the *exact* time at which he was called upon to make this examination, as this may prove of some importance later in the case in showing whether the woman has taken an early opportunity of presenting her claim and may, on the other hand, prevent the accused assailant from setting up a false alibi in the case. The physician should get as much information as possible as to the nature of the assault, the place, the exact time, and the woman's story of the resistance offered by her. He should then proceed to make his examination, noting any and everything that may possibly have any bearing on the case, special attention being paid to the signs of violence about the genital organs and upon the body of the woman. It must be repeated in this connection that the examiner must be extremely careful not to make an examination or to attempt so to do without the consent of the woman, as such conduct on the part of the physician constitutes an assault. No court order is sufficient to overrule this power of refusal on the part of the woman, but it is probable that her refusal would tend to cast suspicion on the truth of her charge of assault. If she has actually been raped, she will be, or should be, anxious to have her charge corroborated; but if she is trumping up a false accusation, then she will probably refuse to permit examination. However, it must be remembered that false charges of rape against children may be based upon injuries inflicted upon a child by a mother and, in such cases, the mother will be only too anxious to have an examination in order to corroborate her story. The physician must be on his guard and not be misled by appearances. Usually there will be something in the story of the child or the mother that will be suspicious or will be contrary to medical science, so that the fraud may be detected.

The medical evidence in cases of rape may be derived from four sources: (1) Marks of violence about the female genital organs; (2) marks of violence upon the body of the complainant or the defendant; (3) stains of semen or of blood on the clothing of one or both parties to the assaults and (4) existence of venereal disease in one or both parties. Before proceeding with the discussion of these points, it is to be said that in any special case no evidence at all may be obtainable from an examination of the woman, so that her testimony must remain unsupported or unrefuted. In order to form an opinion concerning the question as to whether or not intercourse, partial or complete, has taken place, it is necessary to have in mind what we are to consider as normal conditions in a female that has never had intercourse, remembering that rape may be accomplished by simple penetration and that this may occur with little or no evidence of loss of the signs of virginity.

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[1] State *v.* Smith (Idaho), 265 P. 666.

Signs of Virginity.—It is to be said in the beginning that there is no one sign, which, taken alone, may be said to be absolutely indicative of virginity. It is only after an examination of all the signs that one is in a position to state that a female is probably a *virgo intacta.* It should be remembered that no examination in a case of disputed virginity should be made during the period in which the female is menstruating.

The *labia majora* in their virgin state are firm and plump, their median surfaces lying in close apposition with each other and completely covering the nymphae (*labia minora*), the clitoris and urinary meatus, although the clitoris is occasionally visible before puberty. The position and condition of the labia are not very visibly altered by one or even by several intercourses, so that their normal virgin state may still be present when the examination is made. However, after repeated coitus or after childbirth, the labia are more or less separated and the parts formerly covered now may be readily seen. The *labia minora* in their virgin condition are rose-tinted owing to the protection afforded by the labia majora. However, as the latter lose their close contact and separate more or less the labia minora becomes more or less withered and appear brownish and dry. It is probably true that the condition of the labia majora depends more upon the state of general nutrition and age of the female than upon other factors, so that an examination of these parts will certainly give no definite evidence as to the existence or absence of virginity.

The *fourchette* and *posterior commissure* are very little affected by intercourse, except where more or less violence has been employed, so that their presence in a normal state would show nothing as to whether intercourse had taken place. However, these parts seldom survive a first delivery, so that their rupture would be very strong evidence of the fact that the woman had been delivered of a child, a point of value in certain cases.

The *hymen* is the sign of virginity above all others. While many writers have attempted to prove that it is occasionally absent, yet, as Edgar and Johnstone remark, "it is safe to assume that in one form or another its presence is so constant as to make the few exceptions of little importance." It is probable that it has been reported as absent, owing to its being occasionally deep seated, a persistence of the usual infantile condition. The hymen varies in thickness from one to three millimeters, while its consistence may vary from a soft and elastic state to a firm and almost tendinous nature, the latter type offering a great obstacle to coitus. It should be remembered that it may be so thin and elastic that coitus is possible without its rupture. Its orifice is usually nearer the meatus than the center of the membrane and will usually permit the passage of a finger without rupture of the borders of the membrane, although some types have such a small orifice that they may be regarded as almost impervious without rupture. "There are four principal forms with numberless variations in each; the form of the hymen with a central antero-posterior slit, the semilunar, annular and diaphragmatic. Of these the first and third are more common. The first variety consists of two folds, placed on either side of the opening with a central slit between them, running antero-posteriorly, like a buttonhole. It is the usual shape in children. The semilunar fold is situated with its thickest portion at the posterior commissure and the horns running up the sides of the os vaginae and tapering off toward the meatus. It is, as a rule, very regular and becomes accentuated with the progress of age. The annular form is almost infinite in its variations, but its usual shape is a circular band with a large central opening. It may be shrunken to a mere strip and is then little likely to be ruptured by coitus, or it may close up, leaving only a pin-head opening. This

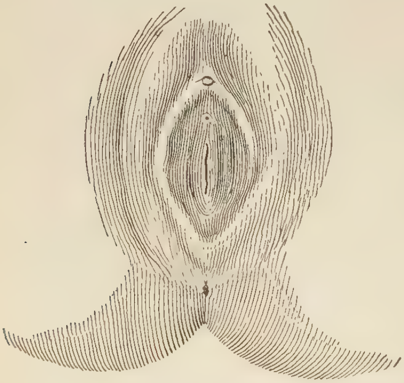

Fig. 27.—Hymen with linear opening. (Tardieu.)

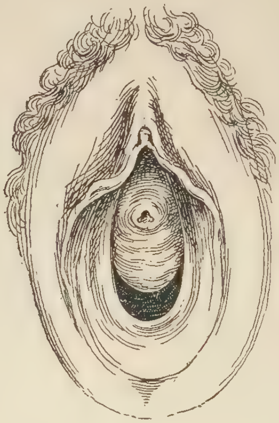

Fig. 28.—Crescentic hymen. (From Chaddock, in Peterson, Haines and Webster, "Legal Medicine and Toxicology.")

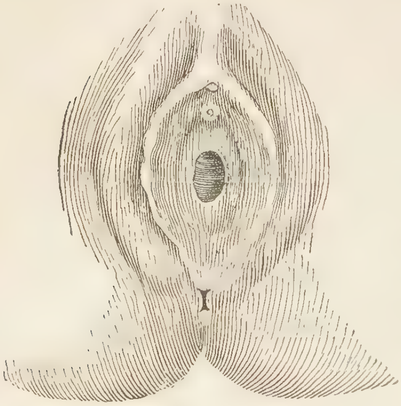

Fig. 29.—Annular hymen. (Tardieu.)

forms the fourth variety, the diaphragmatic. Here, there may be two small apertures on either side of the median line or the membrane may have the appearance of a sieve (cribriform). The edge of the circular membrane may be split by a number of little clefts (fimbriated), which should not be mistaken for the slight tears produced by intercourse. When the clefts become accentuated, as happens in rare cases (Tollberg), until they reach the wall, the hymen is said to consist of multiple folds." (Edgar and Johnstone). The imperforate hymen is to be regarded as a pathological condition and will permit coitus only after surgical procedures. It is important to note, as Chaddock states, "that the condition of the hymen varies with variation in the position of parts about it. It does not present as a tense membrane. With the genitals in their usual position, the hymen is folded on itself. The crescentic hymen has a median anteroposterior fold; the edge of the circular hymen is folded into a cone extending outward. In adults wide separation of the thighs and labia makes the hymen tense, but in children, owing to the greater extent of the hymen as compared with the *introitus vaginae*, it ordinarily remains lax under like circumstances."

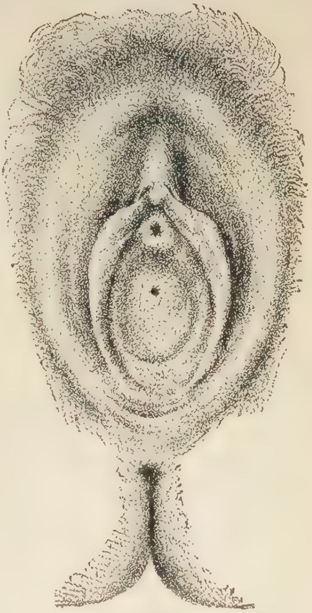

Fig. 30.—Diaphragmatic hymen. (From Witthaus and Becker "Medical Jurisprudence, Forensic Medicine and Toxicology," Wm. Wood and Co., Publishers.)

In cases of alleged rape the question often arises as to whether an intact hymen is positive evidence of virginity. This must be answered in the negative. While it must be admitted that an intact hymen is the most valuable physical sign of virginity, yet it must be granted that intercourse may occur without rupturing or tearing it in any way. The peculiarities of the hymen itself, its elasticity, the size of the opening, and its location must all be taken into consideration before the question can be definitely decided in any specific case. As simple penetration of the genital organs constitutes rape in law, the penetration need not be beyond or even to the hymen. Further, intact hymens have been found repeatedly in prostitutes, and cases are reported of persistence of the hymen after delivery (Stolz), and Budin has collected thirteen cases of primiparae with perfect integrity persisting until confinement and many others have been reported where division of the membrane was necessary before delivery could be accomplished.[1]

Another question of almost equal importance is whether the absence of an intact hymen is to be taken as evidence of non-virginity. While admitting as stated above that the presence of an intact hymen is not absolute evidence of virginity, yet it must also be admitted that an intact hymen is undoubtedly a more certain indication of virginity, than is its non-existence, of a loss of chastity. While the hymen may be more or less torn in the first act of coitus, the rupture being almost invariably accompanied by hemorrhage of a greater or less degree, yet as we have seen such conditions depend upon the nature and location of the hymen. There are many cases in which attempts are made to dilate the vagina in order to render immature girls capable of intercourse, in which procedure the hymen will be ruptured. Further, accidents to the genital organs may produce tears and lacerations of variable extent, while congenital malformations may give the appearance of a ruptured hymen. Surgical operations about the genital organs, as well as inflammatory processes or even medical examinations in these regions, may destroy the hymen.

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[1] See "Rape" by Edgar and Johnstone, in *Medical Jurisprudence, Forensic Medicine and Toxicology*, 1907, **2**, 673.

The *vagina* in the virgin state is small and narrow, presenting marked folds (rugae) of its mucous membrane, but this condition is also noted in healthy young married women, who have not borne children. Childbearing ordinarily destroys these rugae, although Tidy states that they may persist after a single confinement occurring at an early age. Sexual intercourse probably does not alter the virginal condition of the vagina to any extent, although a profuse leucorrhea may destroy the narrow vaginal rugae, increase the size of the canal and render the walls more or less lax, even in those who have never had intercourse. It is clear that an examination of this condition of the vagina could not be made if the hymen was intact and had a small orifice, without causing rupture.

The *breasts* of the virgin are plump, elastic, hemispherical, and non-pendulous, the nipple being at the apex and slightly developed. The nipples are surrounded by a pink areola, which is altered and changed to a darker hue by conception but is not affected by intercourse.

It will be seen, from the preceding discussion that it is not the simplest matter to state that a woman is or is not a virgin, as one must consider all the signs given above before he may venture an opinion. However, the following statement by Tidy, which is an enlargement of an earlier one of Casper, may be taken as a guide.[1] "Not assenting to that unfounded scepticism which has been asserted in regard to this question both in earlier and more recent times, I must declare, that when a forensic physician finds (in a girl arrived at puberty) a hymen still preserved, even its edges not being torn (and more particularly if the aperture be undilatable and of small size, and the membrane itself normally placed, and of ordinary shape, and structure), and along with it (in young persons), a virgin condition of the breasts and external genitals, he is then justified in giving a positive opinion as to the existence of virginity."

Coming back now to the discussion of the evidence furnished by the medical examination, we wish to say that such evidence will depend to a great extent upon the age of the female assaulted and the amount of violence used by the male in committing the assault, as well as upon the time of making the examination.

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[1] *Legal Medicine,* 1884, **3**, 121. See Casper, *Forensic Medicine,* New Syndeham Ed., 1864, **3**, 281.

Marks of Violence about the Female Genital Organs.—If the assault be upon a child the marks of local violence may be more pronounced than in the case of an older female, owing to the usual disparity in size between the male and female sexual organs, although it must be stated that rape in a legal sense may be perpetrated without necessarily producing any marks of violence upon the pudendum of a child. In young children the signs presenting are usually those of incomplete defloration, the hymen almost never being found destroyed although one or several lacerations of the edges of the hymen may occur. In the case of an older child, practically all the signs of so-called rape may be found upon the body, while in adults, who have preserved their virginity up to the time of commission of the assault, or in those who have been long accustomed to sexual intercourse, a few of the signs of rape may be found, provided the examinations is made as quickly as possible after the assault.

It is clear that the degree of injury to the female genitals will be proportional to the force employed and, also, to the size of the female organs as related to those of the male. The external sexual organs will exhibit inflammatory symptoms varying from a slight sensitiveness to a swollen, hot, congested state together with slight excoriations of the mucous membrane and, possibly, ecchymosis, some effusion of blood and laceration of the vulval tissue, especially if the violence be rather extreme. With the adult the inflammatory signs may be slight and the signs of local injury few, but with the child most of the above signs will obtain, owing to the small size of the female organs. If the violence to the child be marked, one may find laceration of the nymphae, destruction of the fourchette and posterior commissure, and, even, rupture of the perineum, along with an almost complete destruction of the hymen and more or less injury to the vagina. Although cases have been reported in which this list of signs has been noted in an adult, as a rule the chief evidence in the adult is obtained from the ruptured hymen. Here it must be remembered, as we have previously stated, that complete intercourse may occur without rupture of the hymen, but this is rather infrequent, except with young children. The deep situation of the hymen and the narrowness of the pubic arch and of the soft parts in the case of children prevent the introduction of the penis and protect the hymen, while with the adult complete coitus may occur with no rupture of the hymen. In recent cases blood may be oozing from the abraded surfaces and clots of blood may be found in the vulval tissues especially in adults, but are generally absent in young children owing to the fact that the penetration has not ordinarily been sufficient to cause these effects. Recent rupture of the hymen is not ordinarily difficult to recognize, as the inflammatory swelling and the unhealed edges of the lacerations remain as direct evidence. Slight lacerations of the hymen ordinarily heal in two or three days, although it may require from 1 to 3 weeks for complete healing of the more severe injuries. Hence, at any time before healing has taken place the diagnosis of rupture of the hymen and, hence, of possible rape may be made, but it is a very difficult matter to assert positively that a rape has been committed if the examiner is called upon at a much later period, as is usually the case. As Casper remarks: "But the decision of this question in medicolegal practice presents another difficulty in the circumstances that almost in every case the examination of the party said to have been abused, as may be readily understood of a matter proceeding from the police to the law courts, has to be undertaken by the medical jurist at a period so long after the commission of the deed that often the most decisive effects upon the body are obscured or completely obliterated." While a recent defloration may be fairly definitely established, provided the examination be made within a few days of the assault, a non-recent defloration may be determined chiefly by the absence of a complete hymen and the presence of remnants, although rupture from other causes than coitus must be remembered. However, if healing be complete it is probably impossible to state anything as to just when the defloration took place. If cicitrization of the lacerations has been perfect, the lines may be brought out by passing the finger behind the folds of the ruptured hymen and drawing it forward to obliterate them. The edges of the hymeneal tears are smooth and rounded from the formation of scar tissue. Along with this condition of the hymen, we may note, some time after the assault, a dilated and patulous condition of the ostium vaginae as well as of the vagina itself.

As the parts involved are in an acutely inflamed condition as a rule following an assault, especially one with violence, walking becomes difficult and painful and any attempt to separate the thighs for the purpose of making an examination of the parts causes great pain. These signs are especially indicative of recent intercourse in one unaccustomed to it, although by themselves can not be regarded as anything more than corroborative of the woman's story of an assault. Under such conditions it not infrequently happens that an examination is not always possible and it may become advisable to make a second examination after the acute inflammation has subsided, in order that a definite statement may be made as to the condition of the hymen, although for purposes of evidence it is always wise to do as much as possible at the first examination or, at least, at the earliest possible moment after the attack, for self-evident reasons. Devergie has very correctly said "En matière de viol une defloration est deja ancienne au bout de 9 à 10 jours."

Besides the above signs we may notice, as a result of the violence to the tissues, a mucopurulent discharge of a yellowish or greenish-yellow color and more or less viscous. "This discharge is extremely important, since it is almost constantly found specially and particularly in children from the twelfth to the fourteenth year, whenever the genital organs have met with any rough usage by an attempt at rape or otherwise."

Such a discharge is more often assumed to be evidence of rape upon girls than almost any other symptom. However, it must be remembered that leucorrhea is a common affection of childhood and that the discharge may be either catarrhal as a result of vulvo-vaginitis or endometritis or may be even gonorrheal, so that the examiner is cautioned not to be too hasty in attributing the discharge to possible violation, especially should there be no evidence of injury to the genital organs. The discharge caused by violence will ordinarily disappear in a few days, unless an intercurrent gonorrheal infection has been present or has been transmitted by the coitus, while true catarrhal conditions of the vagina or uterus run a much more chronic course. In all cases an attempt should be made to ascertain whether or not a discharge existed before the alleged assault.

Marks of Violence upon the Body of the Complainant or Defendant.—It is evident that, if much resistance is offered by the woman, there will be found signs of the struggle in the form of scratches, abrasions, contusions, and even severe injuries located especially in the region of the genital organs, the thighs, abdomen and perineum, but occurring in other localities depending upon the type of the struggle. Such marks of violence are rarely found in children as the resistance offered by them is usually slight, so that it is an easier matter for the male to accomplish the rape without inflicting much injury outside of the pudendum. As stated above, rape may be accomplished on a child without leaving any signs of injury on the pudendum, so that in such cases the medical examiner has nothing upon which to base his opinion. This fact has been well expressed by Taylor as follows: "When there are no marks of violence or physical injury about the pudendum of a child, whether because none originally existed, or they existed and had disappeared in the course of time, a medical witness must leave the proof of rape to others. He can only answer questions of possibility or probability, according to the special facts proved. It is, however, in all cases his duty to be guarded in giving an opinion that a rape has been perpetrated when there is a total absence of marks of violence on the genitals." It is also interesting to note from the analysis of 200 cases of rape studied by Edgar and Johnstone that marks of violence were found in nine cases only, these showing slight injury rather the result of roughness in forcing the thighs apart from a violent effort to overcome resistance on the girl's part. With the adult the injuries may be very severe, as the resistance of the woman may necessitate brutal measures on the part of the assailant. However, even with adults there may be no traces of the struggle shown on the body of the woman. If, then, the signs on the pudendum are slight and no external evidence of violence is found, the medical examiner must be extremely cautious as to his opinion concerning an actual rape. It must be remembered that it is a very easy matter for a woman to produce artificially and intentionally such appearances of injury to substantiate her charge of an assault, so that the physician must not be lead into making statements based on information given to him by the woman or her friends. In this connection Casper lays special stress upon making a psychological as well as a somatic diagnosis, taking the party to be examined by surprise so that she may be unprepared when visited for the purpose of examination. In any case the physician should swear only to what he himself knows and must not be taken unawares by false signs or misstatements of others.

A thorough examination of the accused is usually required in order to furnish evidence at a trial for rape, although in many cases such examinations are not possible until so long after the assault that nothing will be obtained by the examiner, but such examination cannot be made without consent of the accused. If, however, the accused can be examined soon after the alleged rape, much valuable information may be forthcoming. Thus, if the woman were in a position to defend herself, scratches, bruises and even lacerations may be found on the body of the accused, especially on the face, hands and genital organs. The clothing may be torn and may show spots of blood or seminal fluid. Dirt or mud on the clothing of the accused may be of value in indicating that the person was at the scene of the crime and was probably implicated in a struggle on the ground. The male genital organs should be examined for evidence of abrasions, for the presence of blood, and for the existence of possible venereal disease. However, as the alleged violator is not always known and is not located until some time after the commission of the crime, it is very unlikely that much evidence will be obtained from an examination of his person or clothing after time has been allowed to prepare for such emergencies.

Stains of Blood or of Semen on the Parties to the Assault.—Blood is not infrequently present on the genital organs, thighs and abdomen of the woman following a rape, although if the hymen has been ruptured prior to the assault then the violence may be insufficient to cause any hemorrhage. The clothing of the woman and also the genital organs and clothing of the man may also be stained by the bloody discharges, if such there be. However, as we have stated before, whether or not there will be any evidence of blood found will depend upon the time of the examination relative to the time of the assault. Of course, stains of blood will remain upon the clothing and this may be examined at any subsequent period, but there is little possibility of determining whether or not blood was present on the person of either party, if the examination is made some time after the assault, as this will have been washed off unless the persons be of distinctly filthy habits. As to the methods of detecting blood reference is made to a preceding chapter. It should be remembered that it is not uncommon for women to place blood upon their clothing in order to corroborate their story of an assault, so that the examiner will not be in a position to state anything as to the source of such blood unless the woman has made the mistake of using blood of some animal in place of human blood. Menstrual blood may, also, be found on the underclothing of the woman and should not be mistaken for blood arising from an assault, although there is little difference between menstrual and other blood except the possible presence of epithelial cells in the former.

Detection of Seminal Fluid.—In the case of semen, this may be found in and about the genital organs of the woman, on her clothing and especially in the pubic hairs; while the clothing of the male may be stained with it. The presence of semen about the genitals of an alleged victim of rape is most certainly evidence of sexual intercourse, but it can not be taken as proof of rape as it may have come there during a natural coitus with full consent on the part of the woman. The material ordinarily submitted for examination for seminal stains will vary under different circumstances and will usually consist of bedclothing, underclothing and other wearing apparel, fresh material taken from the genital organs, or dried secretions from the genitals, pubic hairs, or even from the thighs of the victim of the assault.

Appearance of the Stains.—The appearance of seminal stains varies according to the nature of the substance upon which they are made. If on a nonabsorbent surface, such as woolen cloth, velvet, or even starched cotton or linen, it forms a grayish-yellow scaly stain; while in absorbent fabrics the material sinks into the meshes of the cloth, forming an almost colorless stain with an irregular outline, the stained portion feeling much stiffer than the unstained part of the cloth. In many cases the seminal stain is mixed with blood or other fluids, so that its nature will not be evident until a thorough examination is made.

Chemical Tests for Seminal Fluid.—Although chemical tests have been introduced for the detection of seminal fluids, it is to be said that none of them are specific as they are given with other body fluids than semen, or with decomposition products of lecithin-containing tissues. However, they do have a certain value in forensic work, just as do the guaiac and benzidin test for blood, in so far as a negative test with them indicates that the stain does not contain seminal fluid, while a positive test denotes that the stain may be due to the presence of semen.

(*a*) *The Florence Test.*—A portion of the dried secretion or of the stained part of the fabric is placed in a small watch glass, treated with a few drops of distilled water, and allowed to soak for a few minutes. A few drops of the watery suspension of the material obtained by the extraction are placed upon a glass slide and are treated with a drop or two of Florence's reagent[1] and at once covered with a cover-glass. If the suspected material contains dried seminal fluid, microscopic examination of the preparation will reveal the presence of many brown rhombic crystals, that resemble the hemin crystals of Teichmann, although they are somewhat smaller in size. These crystals are in the form of fine needles, lance-shaped or ovoid bodies often grouped in rosettes. This test is positive with seminal stains many years old, so that it may afford evidence long subsequent to the alleged assault.

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[1] This consists of 1.65 grams of potassium iodide, and 2.54 grams of iodine dissolved in 30 cc. of distilled water.

(*b*) *The Barberio Test.*—A watery extract of the suspected stain is prepared as stated above for the Florence test. This is then treated with a drop or two of a saturated aqueous solution of picric acid when an immediate precipitate of yellow, sharply refractive, ovoid or needle-shaped crystals appear throughout the microscopic specimen. Stains as old as six years will give this test, but specimens heated to 150 to 200 degrees C. do not yield satisfactory tests. This test is probably not as significant as is the Florence test, as a negative result with it does not necessarily exclude the presence of semen.

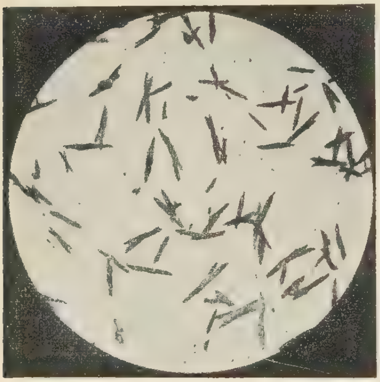

FIG. 31.—Florence test for semen. Microphotograph of crystals. × 150. (From Sydney Smith, "Forensic Medicine," J. and A. Churchill, Publishers, London.)

Detection of Spermatozoa.—The only certain and definite means of recognizing seminal stains is by detection of spermatozoa. It must be borne in mind, however, that seminal fluid not infrequently contains no spermatozoa, especially in cases of old men, so that one may not be able to state positively that a given stain is of seminal origin, as the chemical tests are to be regarded as only presumptive. However, this fact should not deter one from making a careful search for spermatozoa in any given stain.

Spermatozoa are tad-pole shaped bodies having an ovoid head and a tail nine or ten times as long as the head, the latter measuring about 1/3000 inch in length. If the specimen be stained, the anterior third of the head appears less dense than the posterior two-thirds and stains less deeply. Spermatozoa are very resistant to decomposition, so that they may be detected in stains many years old provided they have not been exposed too much to washing or to sun-light. However, they become brittle on drying, so that the head may be easily separated from the tail portion. One should, nevertheless, make careful search of his preparations for the complete spermatozoa, as certain spores may resemble the heads and various fibers may simulate the tails.

In making preparations for microscopical examination proceed as follows: Transfer some of the scaly material, if this be on a non-absorbent surface, to a glass slide and treat with a few drops of water, allowing it to soak for a few hours. If the stain be on absorbent fabrics, cut out, from near the center of the stain, a few threads of the cloth, place on a glass slide and extract with a few drops of water for a few hours. After this extraction the threads may be carefully pressed with a teasing needle and the thread removed. The moist material may then be examined directly under the microscopic, when the characteristic spermatozoa will be observed. If one wishes to stain the spermatozoa, the moist preparations prepared as above may be carefully dried upon the slide and then stained with an eosin solution, the heads taking a deep red tint, while the tails show a light reddish shade. If the preparations are carefully made, one will be rewarded as a rule with positive results showing at least a few fully-formed spermatozoa. Hektoen and Rukstinat[1] advise the following method of staining spermatozoa on cloth: Soak the stained cloth in 1 per cent ammonium hydroxide solution in water for from 12 to 24 hours. After this soaking boil the cloth for 1 minute in water; select a single thread and stain 2 minutes in 5 per cent. aqueous solution of erythrosin; wash quickly in distilled water; stain with 10 per cent. aqueous solution of ferric chloride for 2 minutes; transfer directly to 2 per cent. aqueous solution of hematoxylin for 2 minutes; wash quickly in distilled water; transfer to 0.5 per cent. aqueous ferric chloride solution and tease out the fiber to its finest shreds. Remove from this solution when threads are reddish pink or light brown; wash quickly in distilled water; dehydrate in absolute alcohol; mount in balsam. If the stain has been properly made, the head of the spermatozoon is from a dark purple to black in the posterior two-thirds, while the anterior third is pink, and the tail is from a pink to lavender. The threads of the cloth may stain more or less pinkish.

FIG. 32.—Human spermatozoön: fresh specimen dried on glass.

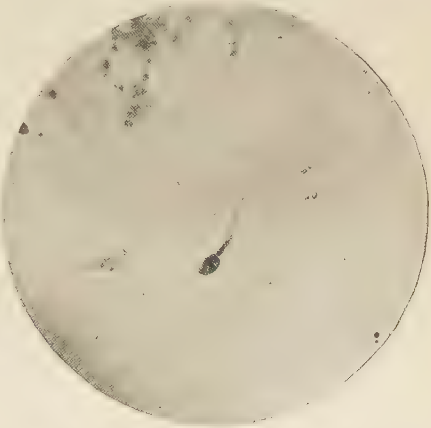

FIG. 33.—Human spermatozoön: from old stain on cloth.

(From Hektoen and McNally in, Peterson, Haines and Webster, "Legal Medicine and Toxicology.")

The Biologic Test.—In 1901 Farnum[2] proposed a precipitin test for human semen based on the same principles as the similar test for blood.

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[1] Arch. Path., 1928, **6**, 96.

[2] Jour. Amer. Med. Assoc., 1901, **37**, 1721.

He found that the serum obtained from the blood of rabbits immunized against human semen gave a distinct reaction with both recent and old emulsions of human semen in salt solution, and also with human seminal stains dried and kept for 34 days. Hektoen[1] confirmed these results, producing a serum which appears to be not only species specific, but, also, semen specific, that is limited to constituents of the semen of that species. In his work he found that seminal stains on various material were capable of detection by this precipitin test. In many tests of blood, serum, pus, ascites fluid, soap, sputum, and seminal-prostatic fluids, dried on cotton cloth, the treated antiserum gave positive reactions with the extracts in salt solution only of the spots containing seminal-prostatic fluid. It seems clear, therefore, that this test promises to be of practical value in detecting the presence of human seminal protein in suspected spots and stains.

Existence of Venereal Disease in One or Both Parties.—It is, of course, evident that venereal disease may be transmitted by a rape. It is necessary, therefore, to examine both the complainant and accused for evidences of such infections, as one or the other may be afflicted with either gonorrhea or syphilis. Should the woman be shown to have gonorrhea, for instance, and a claim should be made that this was contracted at the time of the assault by the accused, the absence of gonorrhea in the male would be probable evidence that he, at least, was not guilty of the rape in question. However, should the male have gonorrhea and no signs of this be present in the woman, this could hardly be taken as evidence that the man had not committed rape upon that particular woman, as gonorrhea is not necessarily contracted by intercourse with an infected person, although it usually is. If, after a sufficient period of incubation for either gonorrhea or syphilis has elapsed, both parties are found to be suffering from the same venereal disease, it may be regarded as highly probable that the accusations of the woman are true. If, on the other hand, the woman shows signs of either gonorrhea or syphilis at an examination made shortly after the alleged assault, it is clear that she must have contracted this at some period prior to the assault. It should, perhaps, be mentioned in this connection, that gonorrhea or syphilis are not infrequently transmitted to young boys by women, who have had intercourse with them by force, or in other words who have committed rape upon the boys, a crime which is apparently not recognized either in English or American laws. The only medical proof of such a crime is the transmission of the disease from the woman to the boy.

UNNATURAL SEXUAL OFFENSES

"Since each author has treated the subject from his individual point of view, clinical, anthropological, or medicolegal, there is far from being unanimous accord as to whether or not anomalies of the sexual instinct are pathological manifestations. The matter of sexual criminality is one that has perplexed magistrates, jurors, lawyers, and medical experts, and has troubled the conscience of judges. Its study, really polyclinic in scope, touches upon questions of social pathology, teratology, mental alienation, and morbid psychology. While history and physiology teach that sexual crimes are marks of weakness and decadence, there is a more recent tendency among scientific men and medical jurists to place them in the category of abnormities, since the facts show that such manifestations ordinarily occur in degenerate individuals in whom the sexual instinct is the point of least resistance. It is now generally admitted that the majority of such cases are owing to hereditary predisposition and that their phenomena are essentially pathological. Different writers also admit that these syndromata of nervous heredity in their different forms may develop spontaneously, or they may be provoked by such agents as the license of literature and the stage, the privation of women, excess and separation of the sexes; and may range over a curious and monstrous field all the way from examples of indecent exposure or exhibitionism up to the hideous crime of profanation of the dead."[1] While we can not discuss the mental aspects of these perverted sexual offenses, which are unquestionably the most important phases, it is well to remember that, in themselves, these offenses are sufficient to raise the question of the mental integrity of their perpetrators, even though, perhaps, they are not to be regarded as a demonstration of irresponsibility. "Sex and sexuality lie in something more than mere physical organs of sex: they enter into the very essence of mentality, and mark it as distinctly with sex as the distinguishing organs of the body. This mental side of sex is commonly spoken of as sexual instinct. The normal sexual instinct is one in harmony with the physical sex and its role in the function of procreation. When the manifestations of sexual feeling or inclination deviate from this normal relation the sexual instinct is said to be perverted. The origin and nature of the perversions to which it is subject can be understood only through a clear comprehension of the circumstances and the relations that attend the origin and development of the normal sexual instinct."[2] Barrett[3] says in this connection: "Abnormal sex impulses are commonly characteristic of those who belong in the class of psychopathic inferiority. Often the qualities of mind that distinguish the psychopathic personality are combined with various physical abnormalities and then distinguish a type of individual who is classed as a 'degenerate.' The position before the law of the psychopathic personality and the 'degenerate' is generally regarded as different from that of the insane. Individuals of these types are definitely abnormal and by reason of this mental difference should not be judged by the same standards as those applied to the healthy normal man."

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[1] Ibid., 1922, **78**, 704. See, also, Hektoen and Rukstinat, Arch. Path., 1928, **6**, 96.

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[1] "Unnatural Crimes: Sexual Inversion: Bestiality, Pederasty, Tribadism" by Rosse in *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 1907, **2**, 737.

[2] "Mental Perversions of the Sexual Instinct," by Chaddock, in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, I, 664.

[3] "Mental Disorders in Medicolegal Relations" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, I, 558.

It is clear that unnatural sexual deviations may take any one of three forms: (1) The abolished sexual function, as shown in the impotence of old age or of those who have been prematurely exhausted by excessive sexual indulgence; (2) the exaggerated sexual passion as shown in *satyriasis* in the male and *nymphomania* in the female; and (3) perverted sexual acts, as shown in uranism, fetichism, masochism, and sadism. The first two of these divisions need no elaboration, as they are sufficiently common to be well known. However, perverted types are the ones that frequently bring the sexual pervert into conflict with the law of the land, although the moral law has undoubtedly been transgressed many times without the offender being brought to justice. By *uranism* is meant sexual passion in which the desire is for an individual of the same sex. This is also known as *sexual inversion* or *homosexuality.* Such morbid attraction is styled *sodomy* if the relation exists between man and man, while if between man and boy it is known as *pederasty*, although, as this type of sexual perversion has reference to sexual intercourse by the anus, it may exist between man and woman. Should the sexual attraction exist between female and female it is designated *tribadism* (Lesbian or Greek love), in which the sexual excitement is obtained by bodily contact and friction, by reciprocal masturbation, or by so called cunnilingus. By *fetichism* we understand the sexual excitement which is brought about by certain parts of the female person other than the genital organs or by association with objects of an insensible nature such as articles of female attire. *Masochism* (or passivism) is that form of sexual perversion in which the sexual desire finds its satisfaction in sexual subjection to degrading, humiliating, or cruel acts on the part of the person for whom the sexual desire is aroused, this person being of the same or opposite sex depending upon whether there is partial or complete psychosexual inversion. *Sadism* is the opposite of masochism, being a sexual perversion in which pleasure is derived from inflicting cruelty upon another. This perversion leads the pervert to beat, humiliate, mutilate, or kill the person for whom the sexual passion is conceived. The most important form of this type of perversion is the so-called lustmurder, which is the basis of many of our most shocking crimes.[1]

Indecent Exposure (Exhibitionism).—This is a mild form of so-called unchaste conduct and consists in such intentional exhibition of the naked human body or of the genital organs in particular as would shock the feeling of modesty or tend to corrupt the morals. Whether or not the exposure constitutes an obscene act depends largely on circumstances, as what might shock the modesty of some would not necessarily tend to corrupt the morals of others, but as decided in one case the nude in art is not of necessity indecent but it may under some conditions be condemned.[1] Exhibitionism is almost invariably dependent upon some mental disorder either permanent or temporary. The persons usually charged with indecent exposure are old men of unsound mind, hysterical girls or women afflicted with imbecility or nymphomania, young men who are intoxicated or suffering from satyriasis, as a direct expression of sexual perversion.

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[1] For a discussion of the psychopathic characteristics of these sexual perversions see Krafft-Ebing's *Psychopathia Sexualis* and Chaddock, *Loc. cit.*

Incest.—By incest we understand the intercourse of man and woman, who are related in any of the degrees which are prohibitive of marriage. Such an act is a felony in many of our states, and is certainly one of the more offensive of the unnatural sexual crimes. It would seem that there was strong reason to investigate the mental condition of the parties to such an act, but it is to be remembered that "the proof of irresponsibility cannot be based upon an isolated act or mental symptom."

Sodomy.—This unnatural sexual offense is, as previously stated, the relation which exists between man and man or between man and woman, intercourse taking place by the anus. As in a charge of rape, it is necessary only to prove penetration of the male organ, it not being necessary to prove consent, no matter what the age of the person upon whom the act has been committed. In such a case the one who affects intercourse (the active agent) is guilty of the crime if the passive agent (the one upon whom the intercourse is practiced) is under 14 years of age; if the active agent be a boy under 14 and the passive agent over 14, the passive agent alone is guilty; while if both active and passive agents are above 14, both are guilty of the crime. While in England this crime is punishable with a sentence of penal servitude, in the United States the punishment is variable. It is to be remembered that the active party may accomplish his purpose by means of physical or moral force and that the passive party may persuade an irresponsible active party to perform the act.

The evidences of sodomy, which the medical examiner may utilize in his efforts to determine whether or not this crime has been committed, are few and not always convincing. As far as the active agent is concerned, it is to be said that there may be nothing indicative of the act in the appearance of the penis, although in some cases there may be abrasions due to the forcible attempt to pass the organ through the sphincter ani. With the passive agent, however, there may in some cases be very extensive abrasions and tears of the mucous membrane of the anus, and, occasionally, there may be serious and extensive lacerations, but such findings are not common unless the force used has been excessive. The more common appearances are (1) a horn-like depression of the nates toward the anus, that is a hollow between the nates, the sides of which converge towards the anus, and (2) a smooth condition of the skin around the anus, instead of the usual folded appearance. These signs are rarely evident except in those who have practiced this habit for some time. Although many writers deny the existence of a funnel-shaped depression of the rectum, Smith[1] finds this extremely prevalent among the sodomists of the East. Further, venereal disease may be communicated by this practice, but this in itself would not be any proof of sodomy, as the infection may have arisen in other ways. The presence of spermatozoa in or about the anus would be strong presumptive evidence of the crime, and stains on the clothing of the victim might be suggestive, but these latter findings would have to be interpreted rather guardedly, as they might have originated in some other manner, unless the passive agent were a young boy. It will be seen from the above that there are no absolutely conclusive signs of sodomy, so that, as Tidy remarks, "A medical witness having found certain of the characteristics described, should not state that the crime of sodomy had been committed, but should depose to certain appearances, etc., observed by him, and be content with stating whether or not they are consistent, in his opinion, with the commission of the crime."

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[1] See United States *v.* Smith, 45 Fed. Rep. 476.

It is to be remembered that the sexual relations between male and male are not confined to the practice of sodomy, or of pederasty in the case of a boy as the passive agent. As Casper points out, "the vice in question is by no means practiced by all as paederastia in the usual sense of the word as immisio penis in anum, but the sexual gratification is obtained by means of reciprocal masturbation." Instead of this practice, a still more disgusting form of sexual perversion is found in the buccal coitus, the so-called irrumation and fellation, about which we will have nothing to say.

Bestiality.—In common law the term sodomy covers, besides the points discussed above, intercourse of a man or woman with a beast. This crime is not a very frequent one, but in the past has been more or less prevalent. Such a practice is, of course, a sign of marked mental depravity, but there have been many convictions of men and boys for unnatural intercourse with cows, mares, and other female animals. Medical evidence is usually of little avail in such cases, as the circumstantial evidence is more conclusive. However, the hair of the animal may be found on the perpetrator, or signs of blood may appear on his clothing and may require careful differentiation as to type. Demonstration of human spermatozoa in the genital organs of the animal would be conclusive proof that such a crime had been committed.

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[1] *Forensic Medicine*, 1928, p. 290.

CHAPTER XV

MENTAL DISORDERS IN THEIR MEDICOLEGAL RELATIONS

It is, of course, impossible in the scope of this work to discuss the subject of mental disorders in anything but the most cursory manner. No attempt will be made to describe the various types of mental derangements with which man may be afflicted, as these are too extensive for anything but the merest reference here. We shall, therefore, limit our discussion more especially to the legal aspects of these subjects as they may influence the consideration of the medical phases.[1]

It must be understood at once that the legal conception of mental disorders, and especially of insanity, is somewhat different from the medical viewpoint and that it is often more or less impossible to reconcile the two views. The medical jurist, however, must realize that he is not responsible for the laws under which questions of mental unsoundness are adjudicated and that he must stick to his own side of the problem. It is undoubtedly true that mental disorders in their medicolegal relations are coming to occupy a much wider field of interest than is included in the relations which have to do with insanity. Much of the controversy, however, in court procedure does center around the determination of sanity or insanity in any particular case, so that we must have some general ideas as to the criteria to be used in determining the presence of sanity or insanity in an individual involved in a legal investigation.

"Mental disorders have medicolegal relations by reason of their influence on conduct and behavior. As the source of all conduct, whether normal or abnormal, is in the functional activity of the mind, alterations of this from its normal or usual workings tend to change the individual in his social relationships. The effects of this may be such as lead to actions and expressions that are harmful to others or violate legal regulations. In these situations mental disorders become problems that must interest the courts and administrators of the laws."[2]

The normal mind expresses itself through the feelings, thought and volition in accordance with the accepted customs and rulings of its surroundings. Just so long as the actions of the individual, as regulated by the functioning of his mind, do not conflict with social relationships or legal requirements, he may be regarded as sane in the eyes of the law; but when the welfare of the individual himself or of the community as a whole is affected by the actions of the individual, then abnormality of the mind must be assumed, provided the conduct of the individual can be shown to be the result of disease, as it would not be strictly correct to imply that all asocial conduct is indicative of abnormality of mind. "Individual man, in his legal relations," says Barrett, "is a member of a social group that has, during its evolution, found it essential to prescribe certain customs and regulations in order to promote the welfare of the group, to provide for its orderly regulation, and to assure safety for life and property. Whatever laws have been made have been formulated upon the view that the normal and healthy man has sufficient strength of will to resist impulses to actions that are punishable, and is able to act with a general appreciation of his rightful relations to others. An individual in possession of these qualities is regarded by the law as sane and is responsible for his expressions and conduct. When the mind is incapable of performing its functions according to normal standards by reason of a defect or disease, and as a result the understanding of the individual of his relations to others and to his environment is abolished or impaired, and normal control of his conduct is lost, then the individual is to be regarded as insane."

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[1] I am indebted to Dr. H. Douglas Singer for many valuable suggestions as to the subject-matter of this section.

[2] "Mental Disorders in Medicolegal Relations" by Barrett, in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, 1, 518.

Mind is represented by mental action, which is manifested through the feelings, thought and volition. "Mental action can only be understood or appreciated by its expression in the feelings generally and their subdivisions, the various emotions; and by thought, which is represented by perceptions dependent in every case on the special sense impressions received into consciousness. Under the head of thought, therefore, must come ideation, which depends on the reception of perceptions, their retention or memory, and their comparison and association, or judgment. The knowledge whether or not thought exists in the individual depends on its expression, either in language or action, in other words in volition. The combination of the three general faculties of the mind constitutes the psychical functions of the brain. Volition must, therefore, represent thought, as action must be purposive in normal mental function. It is under this consideration that we are able to recognize the great difference between sanity and insanity."[1]

In a baby the stimuli are received, as in the adult, through the special senses, but there is no ideation or volition associated with the response to these stimuli, as the expressions of reaction to stimuli are all in the form of reflex actions. As the child grows older, these stimuli (impressions or perceptions) are gradually associated with a memory of previous stimuli of a similar nature, so that the responses to such stimuli begin to show some purposive trend. The child has now learned that certain stimuli are always associated with pain or with pleasurable sensations and will react to them in a proper manner, simply because it has associated these stimuli with such sensations. There is no actual thought connected with such reactions, the mental action being entirely associated with and expressed by the feelings. In other words, the first evidence of mental function is in the field of the feelings or emotions and these are divided in the early life simply into painful and pleasurable ones, subdivisions of such appearing in later life as those of joy, sorrow, fear, placidity, anger, or excessive mental irritation (temper). All this early mental activity is the result of stimuli received through the special senses, as sight, hearing, taste, smell and general sensibility, under which is included touch, pain and temperature. Thus, a child touching a hot radiator associates the heat with the sensation of pain, as it knows as yet nothing of the difference between heat and cold, but sooner or later it learns to connect the radiator with the sensations produced. In other words, the child does not need to be burned but a few times to learn instinctively that the radiator should not be touched.

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[1] See "Medical Aspects of Insanity in its Relation to Medical Jurisprudence", by Fisher, in *Medical Jurisprudence, Forensic Medicine and Toxicology*, by Witthaus and Becker, 1909, **3**, 152.

As the stimuli through the special senses (perceptions) are repeated, there begins to be an association with former perceptions of a similar nature and the child shows the beginning of memory. In other words, these perceptions have now left an impress on the mind of a more or less permanent character, their intensity depending upon the character of the irritation of the special sense and on the manner of reception into the sentient consciousness, that is, on the degree of attention which the child may have given to the perceptions received. On these two conditions will depend the ability of the child to recall the perception as something that has been previously received. Using our former figure of speech, if the irritation of the special sense of touch, as evidenced by the sensation of pain, is very slight on touching a hot radiator, little memory of the perception will be shown by the child unless the attention of the child was rather firmly fixed on the act of touching the radiator. On the other hand, if the pain sensation was very acute, the attention need not be so sharply focussed on the radiator for the child to associate the radiator with pain and thus refrain from touching it in the future. Comparison of the perceptions received from time to time in the mind of the child soon leads to thought about it or to ideation or conception of what will happen under certain conditions. This must imply memory of former perceptions of a similar nature, that is, the recalling of former perceptions, a process called apperception.

The early responses of the cerebrospinal system to external stimuli are, as we have seen, of a reflex nature, but sooner or later the feelings begin to play a more important role in the process, so that the reactions become more directly responsive to thought and ideation. "In childhood actions are largely controlled by impulses. The child acts in the way his feelings urge. As intelligence is acquired in the experiences of mental development the child learns to control impulses by his intelligence, and the more completely an individual acquires this capacity, the more successful is he in his adjustments to the requirements of life." The establishment of judgment requires a much higher development of the cerebral centers than does the simple association of the perceptions in the mind. In other words, judgment is not developed until the mind has become sufficiently mature to weigh the meaning of the perceptions carefully and to form a definite basis of interpretation as to whether or not a certain response to a definite stimulus is good or bad for the welfare of the individual. Volition, or the will to do certain things, is manifest at an early age, but this volition can not be dependent upon sound judgment until the mind has had sufficient experience to enable it to respond in the proper manner to certain stimuli and to overcome certain innate tendencies of the early mind to react only in such a way as may gratify the desires of the child. All of the early development of the mind is associated with the environment of the child, and the mind simply responds to external stimuli by the desire to have or to do certain things which the child wishes to have or to do. There is no sense of responsibility as to what should or should not be done, the child simply acting on the basis of its own desires. It is for this reason that the law lays down the rule that a child up to the age of seven years is not able, from its past experience, to judge as to the nature of its own acts or to assume responsibility for its actions. The child at such an age has no sense of right or wrong and does not appreciate the fact that it should not appropriate to its own use anything that may come in its way or should not do whatever it may desire to do. So, also, the child of this age has no sense of truth, telling the most plausible stories (lies) with no thought that it is doing anything wrong. The child, up to this point, has not developed any relations other than those which have to do with its own desires or pleasures, no discrimination being manifested as to whether or not a certain thing is something that he should or should not do, either from the standpoint of his own welfare or of his relations to others.

"In order that the stimuli coming to the nervous system may be transformed into psychic material, such as perceptions and ideas, and that ideas formed from the memories of past experiences may be associated together in the processes of thinking, it is essential that there exists the mental state that has been designated as consciousness. When this is not present no psychic activity is possible. In the development of psychic life there early comes a phase in which psychic activities come into relation with a feeling that the events that are taking place within the mind are a personal possession. The relationship that is then formed becomes the 'self' or 'ego' or the personality." Up to this point none of the higher qualities have developed and it is only with the evolution of the Ego into the consciousness that the individual is able to discriminate what is for his own personal good or injury. However, when this stage of development is reached the individual begins to act in conformity with the customs and social relationships of the community and his actions are normal or sane just so long as they do not conflict with such relations. The responses of an individual to external stimuli, as expressed in the feelings, thought and volition, ordinarily take a definite direction in any one person, so that we find that some individuals react in one way, while others respond in another way to the same stimuli. In other words, the consciousness of the individual is expressed by his reactions, these going to make up his personality, individuality, or Ego. With the child, as we have seen, the responses are largely egocentric, that is they are almost entirely centered upon self-gratification, as the child has not yet had sufficient mental experience to consider its reactions outside of self, while the older individual has learned through his experience, (memory, thought and judgment concerning his perceptions) that these self-seeking instincts must be made subservient to the social customs and relationships, rights of others and to the legal requirements. If the adult in his mental activity constantly tends towards self-centered responses to stimuli, then he has attained the so-called "Egocentric Personality", which is but an exaggeration of certain features present in many normal individuals and is especially pronounced in those of an egotistic temperament.

The Ego of the normal individual develops along lines which are characterized by so-called normal or sane responses to external stimuli, as expressed in proper reception of perceptions, sane association, thought, and judgment regarding these perceptions and normal volition to respond to the social, moral and legal requirements of the community in such a way as not to interfere with the welfare of the individual himself or with that of others. On the other hand, in mental disorders we find more or less disturbance of the Ego characterized by a changed reaction to external stimuli, by abnormalities in the reception of perceptions, in the failure to recall former experiences, by the confusing of former perceptions with present objective or subjective perceptions through a wrong interpretation of these impressions in the disturbed consciousness, and, along with these, an inability to resist impulses to do things which are not in conformity with custom or with the law. In other words, there is a disturbance in one or more of the fields of mental activity, that is in the feelings, thought and volition.

DISORDERS OF PERCEPTION

In our introduction to this book we called attention to the fact that individuals differed in their powers of observation due to variations in the acuteness of their special senses. In other words, these differences may be traceable to the individual variations in the accuracy of reception of perceptions and to the special attention which is paid to the different perceptions received. As Barrett puts it: "Accuracy of perception may be impaired by defects of vision, by color blindness, by disorders of hearing or of the special senses, and the memories of experiences might not be in agreement with facts." In normal individuals disturbances of sensation have no permanent influence on further mental functioning, as they are considered in reasonable ways and are not interpreted as being something that they are not. When the perceptions received, however, do not correspond to actual realities and can not be corrected, or at least are not, by memory or thought of previous similar perceptions, then a disturbed consciousness exists and the mind is disordered.

In connection with these disorders of perception, the possibility of malingering must be remembered. While it may be a somewhat easy matter to detect this feigning of disorders in individuals who are ignorant and have no definite conception of the nature and basis of such disturbances, yet in those with more education and intelligence, especially if there is some knowledge of mental conditions, the deception can be detected only by prolonged observation. The medicolegal investigation should certainly cover the possibility of the existence of malingering in doubtful cases, as failure to recognize the true nature of the condition with which one is confronted may account for later differences of opinion when the witness is called into court.

Hallucination.—This is an erroneous perception of something that in reality has no physical basis and, hence, can not make any true impression on the special sense organs. It is a sense perception without an actual stimulus. The probable cause of such a perversion of perception is to be found in a diseased or disordered cerebral state and is dependent upon memory of previous perceptions received through the special sense organs involved. The error is in the lack of interpretation of the irritation of the cerebral centers. These hallucinations may occur in any of the fields of sensibility, occasionally several senses being involved. They are most frequently observed in the realm of sight or hearing. It should be noted that where the special sense is congenitally absent, no hallucinations referable to that sense arise.

"Hallucinations of the visual field occur as objects of simple or complex qualities, such as animals, persons, religious or terrifying scenes, of elaborate situations. In the auditory field they are commonly perceived as isolated words, voices, or noises. They hear the name spoken in conversations or are troubled by unpleasant commands or terrifying threats. Hallucinations of smell or taste are experienced as various odors or tastes of unpleasant or disgusting quality." Vividness to the subject and accepted reality of the perverted perceptions are characteristic of hallucinations. Under their influence the victim may commit some act, which brings him in conflict with the moral or statutory laws. "The forensic significance of hallucinations lies largely in the imperative and compelling force they have upon actions of the individual, and their influence in producing unreal conceptions of persons and objects of his environment. Conduct harmful to others is sometimes the direct result of voices that command the carrying out of some action, or threats when these annoyances can no longer be withstood. When hallucinations are present in association with other evidences of a psychotic disorder it is not necessary to show the direct connection of the hallucinations with an action in question. The existence of disordered perceptions indicates a mental state that makes knowledge of right and wrong obviously different from that of the normal man." It should be remembered, in this connection, that normal individuals may be at times subject to hallucinations. Thus, it is not uncommon for an individual, on suddenly waking from a deep sleep, to have the hallucination that some person is in his room or that he hears definite sounds. Under the influence of anaesthetics, hallucinations are not uncommon, so that we need not be surprised to have false accusations of sexual assaults, for instance, made by females coming out from the narcosis.

Illusions.—By an illusion we understand a false perception of an actual physical stimulus. The error here is in interpretation of the perception received, the difference from an hallucination being that here there is an actual basis for the stimulus, while in an hallucination there is no actual stimulus. In both cases, however, the perceptions are false. In illusions the objects seen or things heard are interpreted as something which they are not. In the visual field the object may be perceived as if it were an insect or animal, while in the realm of hearing actual voices may be regarded as making threatening or insulting remarks. An illusion may be so terrifying or unpleasant as to lead to fear or great agitation, leading the individual to commit some atrocious act. As is the case with hallucinations, illusions are not uncommonly experienced by the normal individual, as, for instance, a person may misinterpret a visual stimulus, on waking from sleep, and may believe that a shadow of a chair is a person in his room. The usual feats of legerdemain seen on the stage are almost entirely based on illusion, as the sole object of the so-called magician is to make one believe he sees something that he does not see, or vice versa.

Delusions.—Although delusions are not in any sense to be regarded as disorders of perception, yet they may be the result of hallucinations or illusions and, as such, are discussed in this connection. A delusion is an unwarranted and unfounded belief, and is the result of defective reasoning as to the interpretation of things, the interpretation being contrary to fact and not in harmony with the environment and training of the individual. In other words, they are false conceptions which cannot be corrected by the reason or experience of the person. "The final result of the process of association or thinking is the formation of conclusions or judgments. Into these enter the material that has been collected by the process of perception and held as memories. If either perception or memories are disordered, the effects of this must pathologically influence the formation of judgments, and the conclusions formed will not be in agreement with realities. Delusions have their origin not in what has been experienced, but in the belief of the individual. Their source is in the feelings and not in logical reasoning. Beneath the formation of the delusion there lie pathologic affective forces that turn the thought from its normal course to interest in ideas that are satisfying and appeal to the personality in spite of their distorted representation of realities." (Barrett).

Delusions vary in character from those of an expansive type to those of a markedly depressive content. "The underlying factor determining the choice of content of the expansive delusion is the euphoric mood, the feeling of personal well being that dominates the emotional state of the personality. The delusional ideas appear as delusions of wealth, of great physical power, of being some person of great renown, etc. They are most commonly observed in the clinical disorders of general paresis, in manic excitement, and in paranoid mental states that occur in dementia praecox, in paraphrenia, and in terminal dementia. On the basis of a sad or depressed emotional state there may develop delusions of a depressive content. In a general way, it will be found, in efforts at classification, that the content of depressive delusions relates either to matters for which the individual holds himself responsible, the causes for which lie within himself, and those in which the difficulties come from the environment. Illustrations of the class of delusions that concern the personal responsibilities of the individual are those relating to moral conduct. In another form the depressive content is centered on problems of physical or mental health. The foregoing types of delusions are characteristically observed in the depressed phase of manic-depressive insanity. They are usually a feature of the depressed mental states with anxiety occurring in the late adult or early senile years and are frequently observed in the depressed phase of general paresis. The other general class of depressive delusions largely concern the relation of the individual to his environment. They chiefly occur as delusions of reference or suspicion and of persecution. A frequent form of delusion developing out of conflicts of personal interests with environmental situations is designated as delusion of jealousy. Delusions may center about the complex that the individual is being deprived of his just and legal rights. This may relate to property to which he believes he is entitled or that he is the beneficiary in some testamentary act and is being deprived by fraud of what should be given him."

The forensic importance of delusions lies largely in two directions. One of these is their effect upon the understanding of the individual regarding realities either in respect to himself or his environment. The other is that their inherent marked emotional emphasis gives them a strong determining influence upon conduct and actions. In respect to the influence of content upon the forensic relations of delusions, the closer this content concerns the immediate personal interests, the more important do they become for determining the mental attitude and conduct. Thus, delusions of jealousy and unfaithfulness, of personal wrong doing, of persecution and injustice, and of affliction with disease, have a particularly strong hold upon the personality and are liable to lead to acts of violence and other asocial conduct. Expansive delusions are in general of far less forensic importance than those that have developed on the basis of a depressed or suspicious mood.

As regards responsibility for acts, either civil or criminal, committed by a person having delusions, the law holds that the delusion shall have special relation to the particular act involved in order to relieve the individual of responsibility. Should the delusion have no connection with the act committed, then the person can not be relieved of his responsibility. Thus, in the famous McNaghten case[1], the court said: "If the accused labors under 'partial delusions' only, and is in all other respects sane, he should be considered in the same situation as to responsibility as if the facts with respect to which the delusion exists were real." This is the basis of the interpretation of practically all courts, but this view often comes into sharp conflict with the medical conceptions of responsibility under such conditions. As Barrett states: "In respect to the influence of the existence of delusions upon responsibility for civil acts or capacity to make a will it is abundantly shown in psychiatric experience that no act of an individual with delusions can be regarded as completely free from pathologic influences that are directly or indirectly in relation with the delusion. The fact that an act in question is not the direct outcome of the delusion does not imply that the one who holds a delusion is mentally capable of being regarded as responsible for the specific act. In respect to the influence of delusions on the question of abolishing the resistance to an impulse to commit a harmful or criminal act, there would seem to be no denial of this when the act is the direct consequence of the delusion. When the direct relation does not seem apparent, the resistances that the subject is able to oppose must be far less than those of one who is normal. The continued presence of delusions, with their strong emotional emphasis for the personality, must in time tend to break down resistances, so that a point may be reached when it is impossible longer to check an impulsive act even if its consequences are known to be wrong."

DISORDERS OF MEMORY

We have already seen that consciousness involves the act of self becoming aware of what is going on in the mind. While ideas and perceptions formed in consciousness are continually being replaced by others, yet those that have once been received are normally subject to recall. However, perceptions and conceptions require more or less time and a sufficient degree of intensity to assure their reception into consciousness. It is common knowledge that an individual may be vaguely conscious of things that are going on around him, but that he may not be able to describe what these things were as his mind was focussed on something else than his surroundings. Barrett has described this condition in the following words: "Whether or not one becomes conscious of a stimulus, either in the form of a new perception or an idea previously formed, depends upon the strength of the stimulus and whether or not the state of consciousness was normal at the time the stimulus was active. Much that is continually coming to the nervous system never reaches consciousness, either because the stimulating influence is too feeble to hold the attention, or because it is not in harmony with the emotional qualities dominating consciousness while it was acting. Thus, much that is experienced is easily forgotten or at least cannot readily be recalled into consciousness. That which is feebly imprinted in consciousness is not able to form any extended associative relations with the material that lies latent and thus is difficult to reawaken in the usual course of thinking." It is clear, therefore, that disorders of consciousness may influence the material that is preserved as memory. Normally these memories must agree with actual realities, as received through the perceptions, but if the perceptions and ideas evolved therefrom are not presented clearly owing to abnormality of the receptive centers, then the memory of these perceptions will necessarily be erroneous and may form the basis of delusions. It is to be remembered that retentive memory may be disturbed in organic disorders of the brain without any evidence of disorder of consciousness being apparent.

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[1] 10 Clark and Finnelly, H. L. Cases, 200.

If memories have been preserved they remain latent until recalled into consciousness, but if the retentive capacity has been impaired disorders of recall are always present. "Disorders of memory may be general and involve all perceptions and ideas without selection or may be only for special sensory memories. When the loss of memories involves either some special group of memories or covers a sharply limited epoch of time the condition is designated as amnesia. Amnesia may be total or partial. The amnesia may be for special groups of memory, such as those used in language, producing the clinical disorder designated as aphasia or agnosia when the loss is for those memories necessary for the identification of objects. Amnesia may be of organic or functional causation. Organic amnesia is usually the result of some traumatic injury of the brain or may occur from the destructive influences of a cerebral hemorrhage, softening, or from the effects of a cerebral tumor. More commonly, amnesia is general in its scope and covers what has transpired during a certain period of time in which consciousness was unclear or obliterated. Amnesia may sometimes extend into periods antedating the injury or disturbance of consciousness, and is then designated as retrograde amnesia. Memories that are most recently imprinted are usually least firmly fixed, and, consequently, those that have been retained from experiences in close proximity to the injury or disorder are more readily lost than those found in periods more remote."

DISORDERS OF THE FEELINGS

Feelings are subjective phenomena, which have their source either in instinctive reactions that are an inherent part of the nervous constitution of an individual or in the personal experiences of the person in question.

In this latter case they represent the personal responsiveness of the individual to situations, or ideas, or to changes in the physical relations of the body. "To distinguish more precisely the aspect that feelings have in psychological processes the term affect has come into general use to designate the brief subjective changes of sensation of which the individual is conscious as mental processes are active. In contradistinction to those functions that are classed as intellectual those that primarily concern the feelings are designated as the 'affectivity.' Affects give energy to mental experience and their influence extends through all psychologic functioning. In general, affective reactions are experienced by the personality as either pleasant or unpleasant qualities." Feelings have an influence upon both physical and psychic processes, in the physical field determining the attitudes and expressions of the body and forming the energizing force which controls behavior, while in the psychic realm disturbing the normal clearness of the mind even to complete abolition of consciousness. "Memory for periods during which affects of strong intensity were active may be impaired or abolished. Affective influences very largely determine the choice of ideas that enter into consciousness, ideas come and go in relation with changes in the affective setting. Affects have the quality of spreading out from a primary source on to other events or details that were associated with this, and thus give to the entire experience a common feeling quality. This is designated irradiation or transference of feeling. Not only do affects of qualities pleasing to the personality favor the arising into consciousness of ideas that harmonize with these feelings, but ideas of strongly displeasing qualities may be repressed and excluded from ready association in consciousness."

Affects are ordinarily of relatively brief duration, but at times feelings of the same quality persist for longer periods, in which case they are called moods. Affects have a tendency to find outlets in action, these actions being easiest determined along lines that harmonize with personal feelings and being especially difficult to inhibit when they have affect qualities strongly appealing to the personality. In other words, "One is attracted toward that which is wished for and avoids what is disliked and feared." It is possible, as Barrett points out, that the quality of some affects may be such as to make this resultant action impossible, as repression must be exerted. "The effect of this is to produce tensions that are unpleasant for the personality. When no longer bearable they may find release in explosive outbursts that may produce behavior of definitely pathologic quality. In congenital stages of mental deficiency such as idiocy and feeble-mindedness there are varying degrees of diminished emotional responsiveness. This shows most prominently in a lack of concern for their relations to others. Even where there is no intellectual deficiency affective dullness may be a characteristic of abnormal types of individuals who show qualities of personality that has led to their being classed as 'degenerate'. Lack of emotional responsiveness is a characteristic of that variety of mental abnormality that has sometimes been designated as 'moral insanity'. It occurs as an accompaniment of the deterioration resulting from organic disorders of the structure of the brain in general paresis, the senile psychoses, cerebral arteriosclerosis, epilepsy, and some forms of alcoholic mental disorders. It is a characteristic occurrence during the progress of the deterioration of dementia praecox. In neurasthenia it may show as a more or less indifference or concern for personal responsibilities. Transitory lessening of affective responsiveness is not infrequent in some of the reactions of hysteria. An increase in the normal feeling reactions is a characteristic of some types of psychopathic personalities and hysteric temperaments. In epilepsy there may be an irritability that shows itself in strong outbursts of feeling or anger. This may so overwhelm the consciousness that normal capacity for deliberation is excluded and actions are carried out without control by normal inhibitions."

"The two most common forms in which pathologic disorders of the feelings occur are emotional depression and euphoria. Emotional depression is a usual accompaniment of all painful experiences. Normally this is but transitory and the average mood of the individual is soon reestablished. It occurs as a more or less transient state in general paresis, arteriosclerotic mental disease, and dementia praecox. It is the outstanding symptom in the depressed phase of manic-depressive insanity, and in some types of psychoses occurring in the later period of life, commonly classed as melancholia. In these relationships it may be the underlying influence determining acts of violence against self or others.

"One of the most frequent and well characterized forms of abnormal feeling reactions is what is designated as anxiety. This occurs as a feeling of apprehensiveness associated with sensations usually of tension in the precordial region. It may be an incidental feature in psychoses, such as states of mental depression or epilepsy. It is especially met with in the psychoneuroses, where its origin seems to be in relation with the pathologic influence of affects coming from ideas that have been repressed from consciousness. The anxiety attacks sometimes are manifested in localized symptoms referable to various bodily organs and functions such as respiratory difficulties, asthmatic attacks, functional disturbances of the heart, or disturbances of the normal secretions and excretions. By transference the anxiety may associate itself with ideas of special situations or actions, and in this way may appear as phobias or fears, such as fears of crowds, closed places, or particular situations. The anxiety may be of a degree that impairs the capacity of an individual to understand a situation in a normal way and may be so overpowering as to abolish normal inhibitions to an impulsive action. If the attack has disturbed the clearness of consciousness there remains afterward a more or less impaired memory for the experience.

"Euphoria or a state of emotional exhiliration is a characteristic feature of the manic phase of manic-depressive insanity and of some types of general paresis. It occurs in the early stages of alcoholic insanity and from the effects of some drugs such as morphine and cocaine. It is of importance in forensic relations as an evidence of the existence of a psychotic disorder that might exclude capacity for normal responsibility. With a euphoric mood, especially in manic excitement, normal inhibitions are usually pathologically decreased and actions occur without normal control. In respect to civil responsibilities the euphoric mood, especially in general paresis where it is combined with impairment of judgment, may lead to wasting of property and resources and injury to the rights of others. The importance of pathologic affective influences in relation with criminal actions is seen in their production of abnormal types of character that cannot be judged by the standards applied to the normal man and by the acute effects of these in disturbing consciousness and impairing normal inhibitions. In respect to capacity for civil responsibilities pathologic disorders of the feelings may prevent normal understanding and judgment as to financial and property matters and a regard for the rights of others. In judging the thought and actions of children it must be appreciated that their affective reactions, even within normal limits, are different in intensity and quality from those of adults."

DISORDERS OF THE IMPULSES

Feelings are prone to express themselves in actions, which bring relief to tensions under which the individual labors. Feelings associated with an urge to action are designated as impulses. Impulses are originally independent of ideas, existing as feelings and later, during the development of ideas and intelligence, becoming intimately associated with them. Impulsive actions differ from voluntary actions in that they are not matters of choice but are determined by an impelling motive or urge to do something.

"Those impulses that have their source in fundamental physical and mental needs of the individual stand apart from all others in the importance of their relation to problems of action and conduct in the environment in which he exists. These largely concern problems of self-preservation and are represented in the impulses serving purposes of nutrition and those related to the sexual life of the individual. When impulses are quantitatively and qualitatively different from those of the average individual they are classed as abnormal impulses. If abnormal impulses lead to conduct that disturbs the rights of others and is in opposition to the laws they become problems that have forensic relations. The abnormality of the impulse itself, if it does not find expression in actions, is not a matter that directly concerns the law except as it may be an evidence of an abnormal mental state that apart from the impulse itself may have relations with problems of conduct.

"If consciousness is disordered or if there exists a derangement of mind, that impairs or abolishes the capacity to reason and form decisions, actions may take on an impulsive character. Such a condition has sometimes been described as 'impulsive insanity'. The need of the individual to find for himself relief from tensions and discomforts, arising from affective abnormalities, commonly leads to the association of impulses with some agents or experience that will accomplish this. This association is frequently in relation with intoxicating liquors or drugs, and in this way there become established habits in which the impulse finds expression. Impulses associated with alcoholism and drug addiction frequently come into relation with conduct disorders with which the law must deal. Both alcohol and drugs may produce psychic disorders that exclude the capacity to reason as to the nature and relations of an act or to control conduct. Their influence upon character is such as to lead easily to criminal acts. Sexual crimes are often committed under the influence of alcohol or because of its deteriorating effects, and aggressive acts in the form of assaults and homicide are not infrequent. Alcohol and drug addictions as they are associated with abnormal impulses are frequently matters of forensic importance. Both of these usually acquire at some stage the quality of irresistible impulses. The difficulty is in establishing when they became irresistible. At one period there must have been a time when the impulses could have been resisted."[1]

Probably the largest number of legal problems relating to pathologic impulses have to do with sexual abnormalities. It is undoubtedly true that sexual impulses are expressions of normal instincts of the individual, but these impulses have undergone modifications and restrictions during the development of society. The adult, who is mentally normal, must be able to control his actions resulting from sexual impulses or conditions disastrous to social order would be created. As forensic problems sexual impulses become important only as they become abnormal and result in actions that bring harm to others or tend to lower the moral and ethical standards of social life. The difficulty here is to determine what we are to regard as abnormal sexual impulses and actions, as there is wide variation, both qualitatively and quantitatively, in the sexual activities of normal individuals. "A decrease or absence of normal sexual impulses is not uncommonly observed among the insane and from the effects of the chronic use of alcohol or morphine. A pathologic increase of sexual impulses is an accompaniment of some forms of insanity and in those who are of psychopathic constitution."

The question as to the irresistible quality of an impulse is one that is extremely difficult to determine and little credence is given to this doctrine in courts of law. Whether or not the conduct of the individual was the result of an impulsive action or of conscious choice rests largely on the statements of the individual in question, but it must be remembered that his actions must be considered in relation to the act committed and, also, in association with his other actions prior and subsequent to the questionable act. While such mental disorder as makes it impossible for an individual to resist the impulse to commit some act, which he may or may not know is contrary to the law, will relieve the individual of responsibility for his act, yet it must be remembered that such natural passions as anger or jealousy may so excite a person as to lead him to commit a crime, but these will not excuse a person from criminal responsibility.[1] Barrett discusses this phase of the subject as follows: "The problem that is presented to the psychiatrist in the consideration of the forensic aspects of an abnormal impulse is to give his decision as to whether or not the impulse that leads to an action in question was one that was irresistible and hence would relieve the accused individual of his legal responsibility for an illegal action. The proof that an impulse is of abnormal quality is not proof that it was irresistible. It must be supposed that many an abnormal impulse does not lead to action. It is not probable that the abnormal act of which one may be accused was the first expression of that individual's abnormal impulses. Many of these must have been previously resisted. Each individual case must be judged by itself. The capacity to resist is a relative matter and must vary with conditions of health and disease, both physical and psychic. It is possible for one who suffers from abnormal sexual impulses to have in full health such low limits of capacity for resistance that any lessening of this by disease or any intensification of the stimulus, such as may occur from particular situations, may make the impulse irresistible. The question will come up as to whether this failure of resistance was one that the law recognizes as incapacitating the individual for legal responsibility. Here the only problem that is presented is whether or not there exists in the individual such a defect in intelligence as to prevent development of the inhibitions possessed by the normal man or whether there existed at the time of the action a disorder of mind that made it impossible for the individual to utilize the inhibitions that the normal mind is assumed to possess. If either defect of intelligence or mental disease is shown to exist, then it may fairly be assumed that the impulse was irresistible."

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[1] In this connection, a provision proposed and accepted for inclusion in the new German penal code is of interest (see Berlin letter, Jour. Amer. Med. Assoc., 1929, **92**, 329). This provision is as follows: "If a penalty is imposed on any one who is in the habit of drinking spirituous beverages to excess or of partaking of other intoxicants, because of an act which he committed while intoxicated or which has a casual connection with such habit, or on account of complete intoxication in itself, and his admission to an institution for the cure of the drink habit is indicated, the court shall order that such person shall be placed in such an institution."

MENTAL DEFECT GROUP

Granting that we have abnormalities of mind, as discussed above, it is to be mentioned that we have varying degrees of such mental defects as a result either of congenital lack of development or absence of parts of the brain structure on the one hand and of acquired disease of the brain on the other. Both of these types of mental disturbance vary, also, in degree, so that we have subdivisions depending upon the extent of the cerebral involvement.

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[1] See Guetig *v.* State, 66 Ind. 94; State *v.* Lauth, 46 Ore. 342; and State *v.* Felter, 25 Iowa, 67.

The mental defect group comprises those cases in which actual maldevelopment of the brain has existed from birth or from a very early age, either as a result of definite absence of cerebral structures or of inflammatory processes or defective blood supply to the cerebral areas. "From birth, as a rule, or from disease in early childhood, before the mind attained much degree of development, an accidental or degenerative condition of the brain prevents its natural evolution, so that the faculties which in normal childhood develop by observation and imitation either never develop at all, or else so slowly as to keep the individual in a class by himself." To this group is given the legal name *dementia a nativitate vel naturalis* in contradistinction to that applied to the insanity group (*dementia accidentalis vel adventitia*). It is stated that at least 1 in every 250 of the population is a mental defective, a statement which would seem to be borne out by the experiences of the examining boards during the World War. These defectives are not only a care upon their families but are becoming an increasing burden to the community at large. As stated by Peterson and Jelliffe[1]:" No one has yet endeavored to estimate the cost of the keep of the 10 per cent. of these that are under custodial care, and as for the moneys spent by the community to keep the police and legal systems going, nearly one-half of the necessity for which is bound up in the feeble-minded problems, this is staggering, even to the actuary."

This group is divided into three general classes: the idiot, the imbecile, and the feeble-minded or morons. "Although medical science sees only a series of gradually varying forms, legal procedure needs sharper lines of distinction drawn between the terms idiocy and insanity, as well as between all qualitative words that describe an individual as being imbecile, feeble-minded, or a natural fool, and such terms as define his state as being demented or crazy."

Idiocy.—In this class belongs that group of mental defectives which grades one or two years of age by the psychologic tests of the Binet-Simon type. It is a defect either from birth or from such an early age that there is no mental development. The idiot is not able to adapt himself to the simplest environment or to care for the most common physical needs. "The idiot proper is one who is able to give little or no care to his person, who is barely able to express his material wants, and utterly incapable of any intelligent communication. He is often unable to walk or to make coordinated movements because of a great variety of structural defects. The movements of which he is capable are awkward and ungainly; his steps are uncertain, and he does not perceive impediments or danger when he walks. He has little capacity to direct his wishes, and his behavior resembles that of lower animals. The lack of intellectual development is a peculiar physiognomy and utter absence of expression, a vague, unintelligent, unrecognizing look. A state of continued apathy, a lack of all voluntary effort, a total absence of memory, with only a peculiar cry or sound instead of speech, physical stigmata of degeneration, and bodily deformities, including peculiar formations of the skull that are nearly always present—these are the marks that make up the physical and mental picture of the profound idiot." (Peterson and Jelliffe). While the above is to be considered as a typical picture of the "profound" idiot, it must be understood that there may be varying degrees of the mental defect associated with a more or less complete loss of mental activity, while the physical actions may be more or less normal. In some cases, there is even a great aptitude developed for certain things, such as music, drawing, or even for mathematical calculations, as many so-called "idiot savants" attest. There is practically always a complete lack of the higher ethical or moral nature, so that we find that the desires and passions are unrestrained. Such individuals may show excess sexual desires and may commit assaults or may even become so violent as to commit homicide in a fit of anger at opposition.

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[1] "Mental Defect Group" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, I, 639.

Imbecility.—This is a congenital or acquired mental defect, which differs from idiocy in degree rather than in type. "The mental defect is by no means so complete in all cases. It is to be separated from idiocy on the basis of the intelligence tests. The imbecile groups three, four, five, six or seven years of age, as checked up by the Binet-Simon, Terman or other type of scale. Owing to congenital defect or to an effect proceeding from arrested development due to disease or accident, the brain of such an individual is not capable of average development. The imbecile is generally able to take care of his person and dress, attend to his physical wants, to understand what is said to him, to carry out simple orders, and to perform certain routine duties. His physical organization often differs but little from the average standard of the three to seven year old child; and unless paralyzed, the imbecile has the use of his muscles. His countenance is capable of showing emotions, although these are often manifested by mischievous, evil, cunning, silly, or hilarious expressions. They are incapable of receiving abstract ideas, and though they may appear quite intelligent in one line, as, for instance, having musical ability, being able to do difficult problems, or having a remarkable memory or mechanical aptitude, yet in all other respects their judgment and memory are limited. Although speech may be impossible to a somewhat intelligent imbecile, yet, as a rule, the degree called imbecility, as distinguished from that called idiocy, is characterized by the fact that the imbecile has the power to speak with some degree of intelligence, while idiots are incapable of speech, save, perhaps, the utterance of single words. In imbeciles the speech is often slow, hesitating, irrelevant, and purposeless. It takes time for them to grasp a simple idea, and the comprehension, as well as the expression of a complex idea, is beyond them." Such individuals are often utterly devoid of ethical or moral sensibilities and may commit acts of the greatest cruelty. Special talents may be developed to a very high degree, probably more frequently than in the case of the true idiots. An imbecile may work under supervision, but he is not capable of performing such labor as would probably enable him to care for his own needs. He can adapt himself only to the most simple environments and seems to be more or less devoid of proper appreciation of the relations to others and to the responsibilities of life.

Feeble-mindedness.—The feeble-minded individual or *moron* is one in whom there is a mental defect, which is by no means as great as in the case of the imbecile, but which, nevertheless, is such as to warrant care and supervision for their own protection as well as for that of others. As judged by the intelligence tests, such individuals test up between seven and twelve years of age. The higher grades of feeble-minded individuals, the so-called morons, are those that display such a permanent mental defect as brings them into conflict with the moral or statutory laws by reason of their vicious or criminal propensities. While feeble-mindedness and delinquency are very closely related yet as Peterson and Jelliffe remark, "Not all of the feeble-minded are delinquents, however; many make fairly average citizens, or have been considered as such, as witness the many thousand who were weeded out by the neuropsychiatric examiners in the recent draft board examinations. A feeble-minded man may make a strong, efficient hod-carrier, and pass through life, marry, and advance himself without creating any comments on his incapacity; whereas the same lack of mental capacity in one of the family of thinking men and women would, by contrast, set the individual apart from his fellows. The feeble-minded or the higher grade of imbeciles often make trustworthy and devoted servants and may be capable of faithful routine work." Such individuals, are not capable of the higher type of duties, which require initiative and ability to plan their daily routine, although they can do fairly complicated work without any but the most casual overseeing. Some of these persons, however, sooner or later manifest vicious or criminal tendencies, especially of a sexual nature, so that assaults and even homicide occur as a result of their inability to restrain their impulses.

INSANITY

It must be stated, in the beginning of this discussion, that there is much difference between the medical and legal conceptions of insanity. As a matter of fact, "insanity" is no longer recognized as a medical term, the psychiatrist employing it to express merely the legal or social aspects of a mental disease and indicating, by the statement that a person is insane, that the disease of mind is such that the individual is in need of commitment to an institution; while to the courts the term insanity carries the significance "not guilty". While the medical conception has reference to the consideration of disease as the basis of the abnormal behavior of the individual, the legal interpretation has reference, rather, to the point of responsibility for an offense committed.

If, as we have seen, the normal mind expresses itself through the feelings, thought and volition in accordance with the accepted customs and rulings of its surroundings, then it follows that a deviation from such action, in so far as it comes into conflict with customs of the law, will constitute some abnormality of the mind. It is clear that, when an individual shows such perversions of mental functions as we have discussed above and begins to act in opposition to the rights and privileges of others and ceases to have regard for the customs or the laws of the land, he then becomes either criminal in nature or of abnormal mind. The mind, in the broad sense, must be regarded as something more than a function of the activity of the brain, and must be assumed to be a resultant of the activity of the body as a whole with all its inherent tendencies to react in certain ways to stimuli both from within and without. While abnormal behavior, therefore, may be the result of some perversion of cerebral activity, yet inherent hyper or hypo function in some organs may result in over-emphasis of some instinctive or impulsive actions and under-emphasis upon others. Coupled with such conditions must be faults in training and experience, as well as hereditary influences. While the conduct, words, thoughts and feelings of individuals with mental disorders are merely distortions and exaggerations of those of persons who are mentally well, yet it must be remembered that it is very difficult to draw a sharp line between normal and abnormal behavior, as what is normal under some circumstances may be regarded as abnormal under others.

Insanity may be regarded as an alteration in behavior that may arise as a result of disease of the brain, but it must be said that the more modern views do not insist that mental disease necessarily means "disease of the brain". Although the brain is of special importance in conscious activity, yet the mind is not dependent merely on the brain, but is, rather, to be regarded as the activity of the man as a whole and can be studied only by observing what he says and does under the circumstances which surround him. To the psychiatrist the behavior shown may be, in part at least, the outcome of faulty training and experience rather than of bodily disease.

While it is true that the above statements represent the more modern trend of psychiatric thought as regards "insanity", yet to the medical mind in many cases insanity still is always associated with disease of the brain, so that our discussion must take cognizance of this fact. "Sanity exists when the brain and the nervous system are in such a condition that the mental functions of feeling and knowing, emotion and willing, can be performed in their regular and usual manner. Insanity means a state in which one or more of the above named mental functions is performed in an abnormal manner, or not performed at all, by reason of some disease of the brain or nervous system."[1] As Taylor remarks: "In all cases of real insanity the intellect is more or less affected—hence the term *intellectual insanity.* In a medical sense this implies a deviation of the mental faculties from an assumed normal or healthy standard. In an insane person, his language and habits are changed—the reasoning power which he may have enjoyed in common with others is lost or perverted, and he is no longer fitted to discharge those duties which his social position demands. Further, from perversion of reason, he may show a disposition to commit acts which may endanger his own life or the lives of those around him. It is at this period that the law interferes for his own protection and for that of society." While the terms *moral insanity* and *impulsive insanity* appear in legal decisions, it is probable that neither of these has an actual existence in a pure form. "Moral insanity, as recognized by the courts, involves either a disorder of the brain which affects the moral faculties, or produces an inability to discriminate between right and wrong, which has, as a disease of the brain, proceeded so far as to destroy the reasoning faculties of the mind and impair or destroy the volition." Both of these views have received legal recognition, and in some jurisdictions moral insanity is regarded as synonymous with the theory of irresistible impulse, although this latter conception would seem to be more closely related to the impulsive type of insanity. "The mental powers are rarely disordered without the moral feelings partaking of this disorder; and conversely, it is not to be expected that the moral feelings should become to any extent perverted without the intellect being affected." While the older views of insanity laid much stress on the intellectual disturbances, it is no doubt true that at present mental unsoundness is no longer considered as "in essence a disorder of the intellectual faculties. The modern view is that it is something much more profoundly related to the whole organism—a morbid change in the emotional and instinctive activities with or without intellectual derangement. Long before a patient manifests delusions or other signs of obvious insanity, he may suffer from purely subjective symptoms. These are now recognized to be no less valid and of no less importance than the more manifest signs of the fully developed disorder, which may take the form of delusions, mania, melancholia or dementia."

As we have previously stated the medical and legal conceptions of insanity are more or less at variance. From the medical viewpoint insanity is due to disease of the brain, some functions of the brain being more affected than others, yet all being more or less involved or, in other words, to some extent abnormal. Although the mind may be able to act, yet it does so only imperfectly, just as other diseased organs may function to a certain extent even though they may be more or less extensively involved. Perversion of any one of the higher functions of the mind affects all of the other functions, so that it is impossible to have simple perversion of the perceptions, for instance, without having associated disturbances in the memory, feelings and volition. The medical conception involves a consideration of the solidarity of the faculties which compose the human intelligence, so that the legal idea of so-called "partial insanity" must be foreign to this view. With regard to this point Singer and Krohn[1] state: "The tendency to adopt a cause and thus to develop false conclusions with activities appropriate to these conclusions has led to a concept of an insanity limited to some one topic or complex of ideas; and, formerly, much stress was laid on the possibility of a 'partial insanity' or 'monomania'. Today all alienists are in accord in negativing such a possibility. Even though the excitements and incorrect conclusions seem to center around some one subject, the reasoning and judgments on topics apparently unrelated to this complex being seemingly correct or 'normal', yet such isolation of a group of ideas is psychologically inconceivable. All activities are so intimately interrelated, often by associations that result from purely personal and individual experience, that it is impossible to conceive a disconnection between any sets of ideas. The mind is not a thing, divisible into separate compartments or units. It functions as a whole, even though some sets of ideas are more active at one moment than are others."

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[1] See Stephen, *History of the Criminal Law of England,* 1883, **3,** 130.

The legal point of view has special reference to mental disturbances as they affect the conduct of the individual. It is only when the acts of the insane person come into conflict with the customs of the community, with the rights of others or of the laws of the land that the case assumes forensic possibilities. The ordinary individual is presumed to be sane until proven insane, that is he is supposed to appreciate the nature and moral quality of his acts and to know that certain acts are wrong. "To establish a defense on the ground of insanity, it must be clearly proved that at the time of committing the act the accused was laboring under such a defect of reason from disease of the mind as not to know the nature and quality of the act he was doing, or, if he did know it, that he did not know he was doing what was wrong." He need not know that his act was *legally* wrong, as responsibility is determined on the ability to appreciate the moral quality of the act. This knowledge as to the difference between right and wrong must be with reference to the particular act in question and not to right and wrong in the abstract. Further, the question must be considered as to the subject's ability to make such decisions at the time of commission of the act. It is clearly impossible, from the medical point of view, to admit that a person should be so unbalanced just at the moment of commission of a crime as to be unable to comprehend these points and be perfectly sane in mind before and after the act. True this may involve the question of "irresistible impulse", but, as we have shown, it is irrational to suppose that an individual, who is perfectly sane prior to the act, should suddenly become so insane as to act on the impulse to commit a crime, which he knows is wrong. What really happens is that the impulse is not controlled, although the individual has sufficient mentality to control it. These cases of irresistible impulse must be carefully distinguished from those in which an individual, in full possession of his mental and especially his reasoning faculties, acts from passion or anger. This is not to be regarded as insanity at all from the legal standpoint, as there is no mental disease as the basis for the action. In determining the question of insanity under such conditions, reference must be made to the actions of the individual prior to the act. As Fisher remarks: "The absurd travesty of justice and common sense is seen too often in our courts, by which persons are declared insane and irresponsible at the time of the act, although sane at the time of and following the trial. Such conditions lead juries, from fear of allowing the dangerous if not insane man his liberty, to discard the plea of insanity. The commission of certain acts, which are held to be those of an irresponsible person, usually also mark that person as one who should remain in the custody of the State. The fact that he has at one time been capable of irresponsible action of a serious character makes it possible, if not probable, that he will again be subject to a like impulse. We should estimate his condition from his past history as well as from his present apparent state."

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[1] *Insanity and Law,* 1924, p. 74.

The relation of delusions to insanity is definitely established and is often given special weight in legal decisions. To the medical mind, a person may be insane and have no delusions, while to the legal mind insanity and delusions are closely related and the lack of delusions is apt to afford a presumption of the non-existence of insanity. It has been held, in some decisions, that an individual may labor under so-called partial delusions and be sane in other respects. In this connection he "must be considered in the same situation as to responsibility as if the facts, with respect to which the delusion exists, were real." That is, that unless the delusion with which the individual is afflicted affects the act committed or has a bearing upon it, or if true would not justify the act, this does not relieve the individual of responsibility for the act. Such a legal conclusion really means that the person affected with delusions is in reality sane in respects which are not related in some way to the delusion. As Maudsley says, "Here is an unhesitating assumption that a man, having an insane delusion, has the power to think and act in regard to it *reasonably* . . . that he is, in fact, bound to be reasonable in his unreason, sane in his insanity." However, it must be remembered that it is the province of the medical expert to answer the questions put to him from the medical point of view and not to criticise the legal rulings. He is not the one to decide as to the question of responsibility, as this is the province of the jury, but he should point out how far the mental condition of the person accused is affected by disease and how much the individual may be deprived of free exercise and control of his feelings, thought and volition by reason of a delusion which may in reality not be associated with the act in question. Disease affecting one division of the mind must involve, as we have previously pointed out, the integrity of the whole, so that an individual with delusions cannot act normally with regard to his feelings, thought and volition. While the law is unquestionably correct in assuming that a delusion which does not affect the act committed should not excuse the individual from responsibility for his act, yet the mere fact that the person is mentally diseased and does have delusions, even though of remote nature, should indicate more or less irresponsibility and should affect the type of treatment given him.

Herein is found the realm of conflict between the medical and legal points of view. The difficult point lies in determining the question of insanity itself. While the legal view is, as we have seen, based on recognition of the nature and quality of the act committed, whether it is right or wrong and whether the accused knew the difference as related to the specific act, the medical point of view conflicts and this owing to the fact that, according to medical conceptions, a disease of mind, such as leads to perversions of function of the feelings, thought and volition, renders the individual more or less irresponsible for his acts, even though he may know that they were wrong and contrary to the laws of the land. While medical science teaches that an individual may be so affected by irresistible impulses that he has not sufficient power of will to resist the impulse to commit an act, even though he may know it is wrong, yet the law must have proof that the act is really dependent upon such a disease of mind as makes the impulse irresistible and not merely uncontrolled. As Singer and Krohn remark: "The medical expert, in any specific case on trial, must always bear in mind the old dictum of Dr. Ray that insanity in the law covers nothing more than the relation of the person to the particular act which is the subject of the judicial inquiry. The medicolegal problem in each instance is a special problem peculiar to the case at bar and this problem always resolves itself into the question whether there was mental capacity and moral freedom to do or to abstain from doing a particular act."

Lucid Intervals.—By a lucid interval we mean an interval in which the mind of an insane person has, for that period at least, recovered more or less of its normal activity. It is, in reality, a suspension of the active manifestations of mental disorder. "A lucid interval is not a perfect restoration to reason, but a restoration so far as to be able, beyond doubt, to comprehend and do the act with such perception, memory and judgment as to make it a legal act." A person may commit a criminal act while in a lucid interval, in such a case being regarded as perfectly responsible for his act. It is probable that the relation of lucid intervals to civil acts is of more forensic importance than to criminal acts. As laid down in certain decisions, the law presumes that a crime committed by a person who has lucid intervals was committed by him during such an interval.[1] It must be remembered that the law does not recognize that insanity is present for any definite period either before or after the commission of the crime. All that is necessary is that the mental disturbance existed at the time of commission of the specific act. So, if it can be shown that the insane person really did have a period during which his acts were such as to be based upon sound judgment, or, in other words, that there was a cessation of the manifestations of the mental disorder, the individual is responsible for his acts during this period even though he was known to be insane both before and after the act committed. While medical science recognizes the possibility of lucid intervals and admits that the consciousness would be able to reassert itself for periods, which may be short or relatively long, "still it is rarely that we can say that there is a return to a normal state. The emotions still remain affected, the intellect shows evidence of improvement indeed, but were there a complete return there would be no longer a question of insanity at all."

INSANITY AND CRIMINAL RESPONSIBILITY

A crime must be the result of intent, of a deliberate and wilful misbehavior and disregard of the laws. The person, who has a mental disease or disorder which prevents freedom of choice as to his actions, can not legally commit a crime, although the act may be of the same type as one committed by a normal person, because he has not the mental capacity to form the criminal intent which is the essential element of crime. This distinction has given rise to the legal conception of responsibility, the basis of which rests upon the relation of the mental condition of the person to his knowledge of the nature and quality of the act and whether or not he had sufficient power of will to restrain the impulse to commit the act. Criminal law has been evolved to deal with the type of behavior which we call crime, the object of the laws being the protection of the public and the individual.

The normal individual conducts himself in accordance with the accepted customs and laws of his surroundings, exercising deliberate choice as to his actions; while the person who has a well-established mental disorder tends to act in opposition to the rights and privileges of others and to show more or less disregard for the customs and laws of the land, because his actions are the result of a diseased state and not those of direct choice on his part. The normal or sane individual is, therefore, held to be responsible for his acts, that is he is liable to be punished for his acts if such be contrary to the laws. Punishment of the criminal for his act is the only means which the law has for deterring an individual from the commission of a criminal act. It has been a settled principle of the law that a person cannot be legally punished for the acts committed while he is insane, providing this insanity is such as to prevent the individual from appreciating the nature and quality of the act committed and from knowing that it is wrong. It is presumed in law that, when an individual is insane, he is not capable of forming the intent to commit a crime and is, therefore, not responsible for his acts, the law holding that one who is mentally unsound should be protected from the consequences of his acts.

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[1] See Ford *v.* State, 71 Ala., 385.

A person charged with a crime is legally assumed to be sane, this presumption persisting until evidence is brought forth that raises a reasonable doubt of the sanity of the person accused of the crime, although the common law holds every man as sane until *proof to the contrary* is shown by the party pleading insanity as a defense. The insanity, however, need be proved only to the satisfaction of the jury, so that it is more or less generally held that, if from the proof there is reasonable doubt as to the defendant's sanity, he is entitled to the benefit of the doubt, and, consequently, to an acquittal or to a verdict of "not guilty by reason of insanity." Under conditions in which the plea of insanity is raised by the defense, it becomes necessary for the prosecution to show, if possible, beyond a reasonable doubt that sanity exists. It should be noted, in this connection, that in a criminal procedure the defense does not have to establish actual insanity, but only to raise a reasonable doubt. If this doubt exists in the mind of the jury, it is their duty to find the person insane and, therefore, not responsible for the commission of the crime. The legal interest, therefore, is centered in the establishment of responsibility for an act committed. In a recent case, in which the defendant was convicted of manslaughter for killing her husband by throwing burning gasoline upon him, the defendant pleading insanity, an appeal was taken to the Supreme Court of the State, it being urged on behalf of the defendant that the method used to produce death, together with the surrounding circumstances, suggested insanity, so that the burden of proving it should not have been on the defendant. In affirming the decision of the lower court the Supreme Court said[1]: "Outrageous and hideous crimes are often committed. Sometimes it is difficult for humanity to understand why sane men will perform these acts. Certain psychologists and medical experts believe that no mentally balanced man can be guilty of such atrocity; yet, in the application of criminal law, it is necessary for courts to adhere closely to human experiences and the consensus of opinion drawn therefrom. Until some more scientific method is devised by legislation, this must be the policy of criminal jurisprudence. However this may be, there was evidence before the jury upon which it could find that appellant, at the time in question, retained her judgment so that she rationally comprehended the nature and consequences of her act, and was persuaded by anger to do the fatal deed. Thus we cannot say, as a matter of law, that the jury was bound to believe, without evidence on appellant's part, that she there and then must have been 'insane'".

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[1] State *v.* Buck (Iowa), 219 N. W. 17.

It is this situation which leads, all too frequently, to many of the travesties on justice which are found in our courts. It must be remembered, in this connection, that it must be shown, beyond a reasonable doubt, that a person accused of a crime was insane in the *legal* sense at the time of commission of the act, his condition prior and subsequent to the act not being at issue in the particular case. The point is not infrequently raised that drunkenness so influences a person that he does not possess malice toward another, and that it prevents the formation of the criminal intent, which is an essential of crime. It has, however, been decided that drunkenness is no excuse for crime, and is no bar to punishment. Thus, in one case[1] the court said: "The rule is well settled, while the fact of drunkenness in a case like this may be a circumstance showing the absence of malice, it should not be singled out from the other proof, and the jury should not be instructed that it mitigates the offense. One in a state of voluntary intoxication is subject to the same rules of conduct and to the same rules and principles of law that a sober man is."

As the subject of "punishment" for the commission of crime by a sane individual or of the method of handling an insane person, who has committed an atrocious act is constantly before the courts, a few words in this connection may not be out of place. It is certainly true that some method by which the separation of the questions involved in such cases is greatly to be desired. The two obvious questions, in any so-called criminal case, are (1) did the person accused commit the crime in question, in other words is he guilty? And (2), was the person committing the crime responsible for his act, that is was he sane or insane? By the workings of the Briggs Law in Massachusetts, which law was passed in 1921 and amended in 1923, 1925 and 1927, the department of mental diseases is called upon to examine a person indicted for a capital offense and to determine the existence of any mental disease or defect which would affect his criminal responsibility before trial and before any question has arisen as to the defense of the accused by a plea of insanity. The recent California law attempts, also, to separate the question of sanity from that of guilt and provides that the former shall be tried first where a plea is entered of "not guilty by reason of insanity." If, however, the accused combines other pleas with the one relative to insanity, the question of his guilt will be first determined, the accused being pronounced, for the purposes of this trial, as sane at the time of commission of the crime and the question of insanity being considered after his guilt has been established.

There is a tendency in some states to do away with capital punishment for crime, so that, if this is followed out, the question as to whether or not a person found guilty of a crime shall be sent to a penal institution or one found "not guilty because of insanity" shall be segregated in an institution or farm colony resolves itself merely into one of the type of treatment to be given such individuals rather than punishment. Both of these procedures mean treatment of the disorder in behavior, whether it be labeled "insanity" or "guilt." Further, there is, in addition, the protection of society afforded by the segregation of both types of individuals. Just so long, however, as capital punishment exists in the states, the criminal who is found guilty must be punished by death according to the method in vogue in the particular state. With the accused individual, who is found insane and, therefore, not responsible for his acts, the question of possible segregation and treatment for his mental disturbance is of great importance.[1]

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[1] Fleenor *v.* Commonwealth, 298 S. W. 376. See, also, Harris *v.* Commonwealth, 209 S. W. 509, and Lawson *v.* Commonwealth (Ky.), 1 S. W. (2d), 1060.

It is the conflict between medicine and law as to what constitutes insanity, that has lead to so much trouble in the actual trial of cases brought before the courts. The question of insanity in law is a fact to be determined by the jury, so that all that the medical witness can do, when under examination, is to state just how far the mental disturbance of the accused may have influenced the capacity to judge as to the nature and quality of the act and to appreciate the difference between right and wrong. The expert is not called upon to determine the responsibility of the accused, as this will rest entirely on the proof of his legal insanity, so that he should confine his efforts to showing why he believes the accused to be sane or insane, as the case may be. While the tests of insanity are matters of law and of fact, yet the courts can not do without the opinions of medical experts, although they may be prone to discount what is said as to the relation of the condition of the accused to the act committed. As Judge Doe has said: "If the tests of insanity are matters of law, the practice of allowing experts to testify what they are should be discontinued; if they are matters of fact, the judge should no longer testify without being sworn as a witness, and showing himself qualified to testify as an expert."

As previously stated, the law holds that it is perfectly possible for an individual to be insane on some subjects, that is partially insane, and to be sane in all other respects. On the other hand, the medical view is that such a condition of affairs is inconceivable, as the mind must be taken as a whole and perversion of one part must affect the integrity of the rest. For this reason, it is probably impossible to reconcile the two views as to insanity. The medical witness should not attempt to force his ideas upon the court, but should be content with answering the questions put to him, remembering that his function in such cases is simply to show the mental capacity of the accused individual as a matter of fact.

It is clear that the law recognizes only certain degrees of mental unsoundness as the basis for exemption from responsibility and punishment for an act committed. For years the law has been trying to establish a just basis upon which such a question might be adjudicated. Probably the earliest pronouncement of a principle upon which such a decision might be based is that of Lord Hale: "Such a person, as labouring under melancholy distempers, hath yet as great understanding as ordinarily a child of fourteen years hath, is such a person as can be guilty of felony." In other words the test established by this dictum was the test of mentality of a child of fourteen years of age. Later, in the trial of Arnold[1] in 1723, Justice Tracy laid down the rules for determining responsibility in the following words: "It is not every kind of frantic humor, or something unaccountable in a man's action, that points him out to be such a madman as is exempted from punishment; it must be a man that is totally deprived of his understanding and memory, and doth not know what he is doing, no more than an infant, than a brute or wild beast; such a one is never the object of punishment." Here we have the so-called "wild-beast test", which had as a basis the utter lack of understanding and mental capacity. There was no question of so-called partial insanity or deprivation of understanding, nor was there any allusion to delusions as part of the mental disturbance. In the case of Hadfield, tried in 1800 for shooting at George III in Drury Lane Theater, Lord Erskine, counsel for Hadfield, advanced the theory that the fixed insane delusions of the defendant were the direct cause of the attempted homicide and but for these delusions the alleged crime would not have been committed. In other words, "to absolve from criminal responsibility, there must first be delusion, and secondly, the delusion and the act must be connected." There was no attempt, here, to show that, if an individual had a delusion, he was mentally unsound in other respects, a belief that is medically sound but not legally recognized at the present time, the sole point being that if a delusion was connected with the act committed, then the person was not responsible for the crime. Later in the Bellingham case tried in 1812, capability of distinguishing right from wrong in the abstract was made the test of mental unsoundness. Sir Vicary Gibbs, the prosecuting lawyer in this case said: "although a man be incapable of conducting his own affairs, he may still be answerable for his criminal acts, if he possess a mind capable of distinguishing right from wrong." While Chief Justice Mansfield in his charge to the jury in this case stated: "There was a third species of insanity, in which the patient fancied the existence of injury, and sought an opportunity of gratifying revenge by some hostile act. If such a person were capable, in other respects, of distinguishing right from wrong, there was no excuse for any act of atrocity which he might commit under this description of derangement." On account of these various rulings, much confusion was introduced into court procedure.

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[1] See Overholzer, Jour. Amer. Med. Assoc., 1929, **93**, 830.

In 1843, the celebrated McNaghten case[2] occurred, as a result of which the test of responsibility was made a knowledge of right and wrong in relation to the particular act of which the person was accused and, also, limiting this mental capacity to the time of committing the act.

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[1] Rex *v.* Arnold, 8 Hargraves State Trials, sec. 322.

[2] 10 Clark and Finnelly, H. L. Cases, 200.

McNaghten had shot Edward Drummond, mistaking him for Sir Robert Peel, who, McNaghten believed, was persecuting him. Mr. Cockburn, the counsel for the defense, made partial insanity the defense, alleging the specific delusion as the basis of the act of McNaghten, who had shown no obvious signs of insanity in his ordinary conduct and business. The medical evidence in this case was to the effect that "a person of otherwise sound mind might be affected with morbid delusions; that the prisoner was in that condition; that a person labouring under a morbid delusion might have a moral perception of right and wrong; but that in the case of the prisoner, it was a delusion which carried him away beyond the power of his own control, and left him no such perception, and that he was not capable of exercising any control over acts which had a connection with his delusions." Chief Justice Tindal, in his address to the jury in this case stated: "The point which at last will be submitted to you will be, whether or not on the whole of the evidence you have heard, you are satisfied that at the time the act was committed, for the commission of which the prisoner stands charged, he had not that competent use of his understanding as not to know what he was doing with respect to the act itself—a wicked and a wrong thing; whether he knew it was a wicked or a wrong thing he had done, or that he was sensible at the time he committed this act that it was contrary to the laws of God and man. Undoubtedly if he was not so sensible, he is not a person so responsible." McNaghten was acquitted upon the ground of insanity, the court in reality directing such a verdict with the full assent of the law officers of the crown. This acquittal raised such a clamor throughout England that the House of Lords submitted a list of questions to the 15 trial judges, bearing on the question of insanity as a defense in criminal cases. The answers of 14 of the judges (Justice Maule stating his opinion separately) have been applied to the determination of the relation of insanity to responsibility and this common law ruling forms the basis of legal decisions in England and America, although, as we shall see, in certain of our States the theory of irresistible impulse has been added. This legal test of responsibility as it now stands on the basis of the answers of the judges mentioned above is that "To establish a defense on the ground of insanity, it must be clearly proved that at the time of committing the act the party accused was laboring under such a defect of reason from disease of the mind as not to know the nature and quality of the act he was doing, or, if he did know it, that he did not know he was doing what was wrong."

The above rule has been followed in practically all the decisions in England, although in the United States there has been a tendency to bring the law more into agreement with the principles of insanity as held by the medical profession. The doctrine of "irresistible impulse" has found its way into many of the decisions of our own courts, although many of our States do not accept this theory. The medical profession of England has attempted to show that the *obiter dicta* of the English judges was too narrow and did not take into consideration many of the facts known to medical science, especially the point of uncontrollable impulse arising from mental disease. This subject has been presented by committees of the Medico-Psychological Association, as well as of the British Medical Association, and in 1922 a committee, consisting of well-known lawyers presided over by Lord Justice Atkin, was appointed by the government to consider what changes, if any, are desirable in the existing laws when the plea of insanity is raised. This committee recommended that it be recognized that a person charged with an offense is irresponsible when the act is committed under an impulse which he was by mental disease deprived of any power to resist and that in other respects the McNaghten rules should be maintained. In 1924 Lord Darling introduced into the House of Lords a bill to amend the law of criminal responsibility on the basis of the recommendations of the Atkin committee. However, this bill has not as yet been passed. In this connection Lord Chief Justice Hewart has recently delivered a lecture[1] which adopts uncompromisingly the lawyer's view and fails to consider the medical side of the proposition at all. "Criticizing the report of the Atkin committee, the lord chief justice said that if it was accepted, it would be immaterial that the prisoner knew what he was about, or that he knew he was doing what was wrong. But he would still be excused from criminal responsibility if he committed the act under an impulse which he was by mental disease in substance deprived of any power to resist. This suggestion, whatever its merits might be, was not at all a product of the twentieth century. It was really the ancient and dangerous plea of the uncontrollable impulse, which in practice was so difficult to distinguish from the impulse that was not controlled. The doctrine involved two propositions. The first was that there were unfortunate persons who, though they knew what they were about, and also knew that they were doing wrong, were nevertheless impelled, by diseased and irresistible impulse, to commit an apparently criminal act. The second proposition was one of legislative morality or expediency—that these persons, by reason of their number or otherwise, were of such importance as to require or deserve a fundamental revision of the criminal law. If this unfortunate type existed the question remained whether, for that reason, it was just and necessary to entertain or to make a drastic alteration in the criminal law. If this was done, the objective tests for judge and jury would disappear. It would be of little use to explore the evidence in order to ascertain whether, in the particular case, the prisoner was perfectly well aware of what he was doing, or perfectly well aware that what he was doing was wrong. The crucial question would forthwith be whether he was acting under an irresistible impulse. And on what materials, and with what guidance, would the jury be called on to answer that question? Would there be any except the medical opinion, which the prisoner might be fortunate enough to be able to adduce in his favor, contradicted by the medical opinion which might be offered on the part of the prosecution?"

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[1] See London Letter, Jour. Amer. Med. Assoc., 1928, 90, 42.

In the United States the effort has been made in some jurisdictions to have the jury, which is the sole judge of responsibility, determine whether or not a criminal act was in reality the product of mental disease. In many of our states the tendency has been to follow the English rulings, as laid down by the answers of the judges following the McNaghten case, while in others of our states the doctrine of "irresistible impulse" has found its way into the decisions. Thus in Alabama[1] the court said: "We think that the inquiries to be submitted to the jury, in every criminal trial where the defence of insanity is interposed, are these: First: Was the defendant, at the time of the alleged crime, as a matter of fact, afflicted with a disease of the mind, so as to be either idiotic or otherwise insane? Second: If such be the case, did he know right from wrong, as applied to the particular act in question? If he did not have such knowledge, he is not legally responsible. Third: If he did have such knowledge, he may nevertheless not be legally responsible if the two following conditions concur: (1) If, by reason of the duress of such mental disease, he had so far lost the power to choose between the right and the wrong, and to avoid doing the act in question, as that his free agency was at the time destroyed; (2) and if, at the same time, the alleged crime was so connected with such mental disease, in the relation of cause and effect, as to have been the product or offspring of it solely." Much the same line of reasoning was followed by Chief Justice Doe of the New Hampshire Supreme Court in the case of State *v.* Pike.[2] In the Hopps case[3] in Illinois the court stated: "We have come to the conclusion that a safe and reasonable test, in all such cases, would be, that whenever it should appear from the evidence, that at the time of doing the act charged, the prisoner was not of sound mind, but affected with insanity, and such affection was the efficient cause of the act, and that he would not have done the act but for that affection, he ought to be acquitted. But this unsoundness of mind, or affection of insanity must be of such a degree as to create an uncontrollable impulse to do the act charged, by overriding the reason and judgment, and obliterating the sense of right and wrong as to the particular act done, and depriving the accused of the power of choosing between them." That this theory of responsibility is not held in all states is shown by the opinion of Judge Andrews, in the Court of Appeals of New York in the case[4] of Flanagan *v.* People, who said: "We are asked in this case to introduce a new element into the rule of criminal responsibility in cases of alleged insanity, and to hold that the power of *choosing right from wrong* is as essential to legal responsibility as the capacity of *distinguishing between* them; and that the absence of the former is consistent with the presence of the latter. The argument proceeds upon the theory that there is a form of insanity in which the faculties are so disordered and deranged that a man, though he perceives the moral quality of his acts, is unable to control them, and is urged by some mysterious pressure to the commission of acts the consequences of which he anticipates but cannot avoid. Whatever medical or scientific authority, there may be for this view, it has not been accepted by courts of law."

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[1] Parsons *v.* State, 81 Ala., 577.

[2] 49 New Hampshire, 399.

[3] Hopps *v.* People, 31 Ill. 385.

[4] 52 N. Y. 467.

With reference to the theory of irresistible impulse, Becker and Boston[1] state that the courts of California, Kansas, Maine, Maryland, Michigan, Minnesota, Mississippi, Missouri, Nebraska, Nevada, New Jersey, New York, Oklahoma, Oregon, South Carolina, South Dakota, Tennessee, Texas, and West Virginia have explicitly rejected insane irresistible impulse as a defence; while, notwithstanding capacity to distinguish between right and wrong, it has been accepted as a defence in Alabama, Arkansas, Delaware, Georgia, Indiana, Iowa, Kentucky, New Hampshire, Ohio, Virginia, and Wisconsin. In Vermont and Montana the theory has been intimated, but not actually so held. Likewise, in Connecticut, Pennsylvania, Massachusetts and Illinois, court decisions seem to point toward the acceptance of this line of defence.

In the previous discussion responsibility in its relation to insanity has been considered with reference to the time of commission of the act for which the accused stands charged. If the individual should become insane after the commission of the crime and is insane when arraigned before the court, he cannot be tried for the offense while insane, but should be remanded to jail or committed to an asylum until his recovery, when he may be tried for the offense charged. Further, if the insanity develops during the trial, the proceeding must be discontinued and can not be taken up again until recovery of the accused. Should insanity arise after conviction, judgment must be put off and sentence suspended so long as he may remain insane, and execution cannot be carried out should the convicted person become insane after being sentenced.

Insanity and Civil Responsibility

There is much wider latitude of interpretation of responsibility in cases of unsound mind in civil matters than there is in criminal affairs. It is to be remembered that "public policy is thought by the courts of nearly all the states, to require a much more stringent definition of mental irresponsibility (in the criminal law at least) than any man of science would be likely to adopt for purposes of classification." Hence, it follows that a person may be insane from the medical point of view and yet responsible for his acts from the legal standpoint. In adjudging insanity, medical evidence is required in order to establish the fact of existing insanity, but this medical evidence is far from the same type as is required in determining insanity in a legal sense sufficient to relieve a person of criminal responsibility. Here we find again the conflict between the medical and legal conceptions of insanity. As Fisher remarks: "In no way can the great difference between the medical and legal estimate of the fact of insanity be better shown than in the degree of responsibility ascribed to those of unsound mind, in civil and criminal procedure." In civil matters, however, it must be mentioned that the same degree of mental disturbance is not regarded as necessary to relieve one from responsibility for civil acts, as is the case in criminal matters, as legal considerations give rise to different measures of legal competency with respect to different classes of transactions. Mere mental disease in itself will not relieve an individual from civil responsibility, but it must be shown that the mental disorder has affected the reasoning power or understanding of the individual to such an extent that he did not have the capacity to realize or understand the nature of the act, or to deal with the particular business in question.[1]

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[1] "Mental Unsoundness in its Legal Relations" in *Medical Jurisprudence, Forensic Medicine and Toxicology,* by Witthaus and Becker, 1909, **3**, 450.

Contracts.—A contract in civil law is the union of two or more persons resulting in an accordant declaration of the will, with the object of creating a future obligation between them. It is an agreement or obligation, whereby one party becomes bound to another, whether by record or judgment, or by assent, or even impliedly, to do or to omit to do an act. Its effect is to bind the parties by mutual agreements to perform certain acts, usually within a definite period. A contract is enforceable by law and is the expression of the will of the parties concerned. It is presumed that the parties to a contract enter into it only after more or less full consideration of the points involved therein. In other words, a contract is assumed to be dependent upon the capability of the understanding or of the reasoning power of the parties concerned. This ability to realize the nature of a contract entered into is shown by the consent of the parties. The law holds, as an essential element of a contract, that there must be free and full consent of all parties to the contract in order that it be binding upon the persons concerned. Any undue force, whether physical or mental, exerted toward an individual to compel him to sign a contract, removes the element of free and full consent, so that the contract could not be held to be a binding one if obtained under such circumstances. Further, it must be shown that one must be capable of giving this consent, that is that he must have sufficient reasoning power to appreciate the nature of the contract and to comprehend in a reasonable manner the nature of the matter in which he is engaged. As regards the relation of insanity to responsibility for contracts entered into Parsons states: "They who have no mind cannot agree in mind with another; and, as this is the essence of a contract, they cannot enter into a contract. Mere mental weakness or inferiority of intellect will not incapacitate a person from making a valid contract. There must be such a condition of idiocy or insanity as disables him from understanding the nature and effects of his acts and therefore disqualifies him from transacting business and managing his property."

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[1] See Merritt *v.* Merritt, 32 Misc. (N. Y.) 21; Mann *v.* Keene Guaranty Savings Bank, 86 Fed., 51; O'Neill *v.* Nolan, 66 Hun (N. Y.) 631; and Coffey *v.* Coffey, 74 Ill. App., 241.

It is clear, therefore, that a contract made with an individual, who is mentally unsound but who has not been adjudged insane, is voidable but not void, providing the individual had, in reality, no reasonable understanding of the nature and terms of the contract and did not comprehend the specific contract. As Becker and Boston remark: "When a contract is impeached on the ground of mental incapacity of a party, *not previously adjudged incompetent,* the true inquiry is, whether he had the ability to comprehend in a reasonable manner the nature of the affair in which he participated. If fraud or undue influence has been practiced on a person of weak or impaired intellect, other principles apply; but where mental incapacity is alleged, there must be inability to know what the act is to which the contract relates. So long as one possesses mental faculties requisite to transact rationally the ordinary affairs of life, his contracts and deeds will be valid. He must have sufficient intellectual capacity to know what he is doing, but sufficient discernment or education to transact business with prudence and discretion is not required." The relation of delusions to ability to know the nature of a contract entered into is of importance in this connection. If the delusion bears directly on the execution of a deed, the delusion is held to be evidence of insanity and invalidates the deed.[1] While contracts made, as stated above, with insane individuals are voidable, yet if the insanity does not arise until after the contract is made, the party concerned cannot void his contract. The principles of law governing the contracts of insane persons have been stated by the Supreme Court of North Carolina in the following words[2]: "1. The contract of a person not judicially declared to be insane is voidable and not void. If the insanity has been formally adjudicated, subsequent contracts made by such person are void. 2. A party dealing with an insane person, knowing his mental condition, is deemed to perpetrate a fraud on such insane person and on his rights. 3. When a contract with an insane person is executed and completed, and is fair and made in good faith, without notice of mental incapacity, and the parties cannot again be put in statu quo (their original position), such contract is valid and enforceable. 4. However, when mental incapacity is shown, the burden is so far shifted that the agreement will be set aside unless the party claiming under the contract, by proper proof, establishes the fact that he was ignorant of the mental incapacity and had no notice of it which would put a reasonably prudent person on inquiry, and that no unfair advantage was taken, and that the insane person is not able to restore the consideration or to make adequate compensation for it. 5. The same principles that control the contracts of insane persons apply to negotiable instruments."

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[1] See Ferguson Seed Farms, Inc., *v.* McMillan et al. (Texas), 296, S. W. R. 902.

[2] See Wadford *v.* Gillette et al. (N. C.) 137 S. E. R. 314. Jour. A. M. A., 1927, **89**, 994.

Although contracts made with an insane person are, as outlined above, voidable, yet they may not be voided by the individual concerned. Should he be restored to sanity, the former incompetent must elect within a reasonable time either to affirm or disaffirm his voidable contract. In cases in which a deed or conveyance has been signed by a person of unsound mind, neither the grantor, nor his guardian or conservator, can disaffirm the contract of deed in any court, without first refunding the purchase money and expenditure for taxes, as he could not retain the money and recover the land.[1] That is, in order to rescind an executed contract made by an insane individual with one who was not aware of his insanity, whatever consideration has been received must be returned[2] unless advantage was taken of the insane person by having him sign a fraudulent contract. A contract made with an insane person during a lucid interval is valid and binding upon him.

Contracts made with an insane individual for necessaries for himself and family are generally regarded as exceptions to the rules governing other contracts. The necessaries must be supplied in good faith and under such circumstances as would justify their being furnished, but the liability of the insane person is only for a fair and reasonable value and not for a price which might have been agreed upon between the parties concerned. Should a contract be executed between an insane person and another for necessaries, this contract may *per se* be voidable, yet the insane individual is responsible for the necessaries furnished. A husband is liable for the necessaries furnished to his wife and family even though he be confined in an asylum at the time. The law recognizes as necessaries everything that is proper and suitable for his position in life, and includes the usual household articles, food, clothing, etc., as well as medical attendance for the incompetent and members of his family.

Marriage is a special type of contract, by the terms of which one man and one woman voluntarily consent to a union for life "to the exclusion of others." This contract differs from other civil contracts in that it cannot be revoked or dissolved at the will of the parties and ends only with the death of one of the parties or the dissolution of the contract by some legal process. The law holds that it does not require a high degree of mentality to comprehend the contract of marriage and, hence, it may be entered into by persons, who would not be regarded as capable of entering into other civil contracts. However, a person of unsound mind cannot make a legal contract and, hence, cannot form a valid contract of marriage. The mental condition of the parties at the time of the marriage is what determines the legality of the contract and not the state of the mind either before or after marriage. In other words, a person, even though insane, may enter into a lawful marriage contract during a lucid interval. Mere weakness of understanding will not invalidate a marriage, nor will insanity which does not affect the subject-matter of the contract. Thus it has been stated:[1] "A marriage is not to be declared void because of the mental incapacity of one of the parties, except on the clearest and most definite evidence; and but little weight should be given to the opinion of a physician who did not, at the time of the marriage, see or know the mental condition of the party claimed to be insane." The test to be employed "is the capacity of the party in question to understand the nature and obligations assumed by the marriage." Unless the insanity existed at the time of marriage, courts will not annul the marriage, but if insanity can be shown to have actually existed at the time of marriage, it is cause for annulment *ab initio*. Further, a marriage made under these conditions cannot be rendered valid by cohabitation after restoration of the individual to sanity. However, the courts have ruled that marriage with an insane individual is not void if no legal proceedings have been taken, so that a wife becomes entitled to her widow's rights at his death.[2]

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[1] See Jennings *v.* Gage, 13 Ill. 611; Evans *v.* Gale, 17 N. H., 573.

[2] See Morris *v.* Gt. Northern Ry. Co., 67 Minn. 74.

As regards the relation of insanity to divorce or separation of the parties concerned, the practice differs in different jurisdictions. Almost all of our States do not recognize insanity as a cause for divorce. However, in Georgia, Idaho, Pennsylvania, Utah and Washington insanity is now a statutory ground for absolute divorce (divorce *a vinculo matrimonii*), if the insanity arises after marriage. Many of our States go still further than the mere failure to recognize insanity as a cause for divorce and prohibit suits for divorce on any statutory grounds if it can be shown that the delinquency of the party was due to insanity existing at the time of filing the suit for divorce or at the time of commission of the deliquent act. Thus, in a New York case[3] it was stated: "A violation of the marriage contract by an insane husband or wife does not furnish ground for a dissolution of the marriage. Thus extreme cruelty, if caused by insanity, is not a cause for divorce, and the same rule applies to acts of sexual intercourse between an insane husband or wife and a stranger. Insane delusions on the part of a wife who has committed adultery are no defence to suit for divorce, where, when committing adultery, she was capable of appreciating the nature of the act and its probable consequences." Thus, insanity arising after marriage is a complete defense to a suit for divorce on almost any ground. In England, however, insanity of either party is not regarded as a bar to divorce, a rule that is followed only in the states above mentioned. However, a separation (divorce *a mensa et thoro*) will usually be decreed on the ground of insanity, "not necessarily for the fault of a defendant, but often because cohabitation is inexpedient."

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[1] See Slais *v.* Slais, 9 Mo. App., 96.

[2] See Wiser *v.* Lockwood's Est., 42 Vt., 720.

[3] See Stuckey *v.* Mathes, 24 Hun, 461.

Torts.—A tort, in law, is regarded as a wrong, such as the law requires compensation for in damages. It is an infringement of the private or civil rights of a person. "To constitute a tort, two things must concur—actual or legal damage to the plaintiff, and a wrongful act committed by the defendant."

The practice of the courts of England and of the United States varies in regard to torts committed by an insane individual. The common law of England considers an insane person incapable of committing a tort unless it is shown that he had sufficient mentality to understand the quality and nature, as well as the consequences, of the act committed. In our country, an insane person or his estate is liable in damages to an injured person for the torts that he may commit. The damages are limited to an amount sufficient to compensate the injured party for the injury suffered. The basis of this ruling is that where a loss must be borne by one of two innocent persons, it must be borne by the one who caused the loss or damage. It has been held that an insane person is liable for causing the death of another by an act which would be criminal except for his insanity, the redress being a suit for damages to the extent of the actual loss sustained.[1] Although the insane individual cannot be punished criminally, he is, however, liable in a civil action for the tort he has committed. In discussing the case of McIntyre *v*, Sholty, the statements of the court are referred to by Singer and Krohn[2] as follows: "There is, to be sure, an appearance of hardship in compelling one to respond for that which he is unable to avoid for want of control of the reason. But the question of liability in these cases is one of public policy. If an insane person is not held liable for his torts, those interested in his estate, as relatives or otherwise, might not have a sufficient motive so to care for him as to deprive him of opportunities for inflicting injuries on others. There is more injustice in denying the injured party the right of recovery of damages for the wrong suffered than there is in calling on the friends or relatives of the lunatic to pay the expenses of his confinement or to draw on his estate if he has an estate ample for that purpose. The liability of lunatics for their torts tends to procure more efficient custody and guardianship of their persons."

In regard to civil liability of an insane individual for such torts as are covered by libel and slander, the courts as a rule hold that intent and malice are necessary ingredients of such torts, and that an insane individual is not responsible on the ground that he is incapable of intent to commit a wrong. In some decisions, however, it has been held that the insane individual is liable for actual damages for such torts, but that nothing more than mere compensatory damages can be sought,[3] and that insanity may be a defense in mitigation of damages for slander.[4]

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[1] See Jewell *v.* Colby, 66 N. H., 399; McIntyre *v.* Sholty, 121 Ill., 660.; Seals *v.* Snow (Kan.), 254 Pac. R. 348; Parke *v.* Dennard, (Ala.), 118 So. 396.

[2] "Insanity and Law", 1924, p. 277.

[3] See Ullrich *v.* N. Y. Press Co., 23 Misc. Rep. (N. Y.) 168; Williams *v.* Hays, 143 N. Y. 442; Jewell *v.* Colby, 66 N. H., 399.

[4] Yeates *v.* Reed, 4 Blackf. (Ind.), 463.

Testamentary Capacity.—The right to dispose of property by a last will and testament is not regarded as a natural inherent right, but is one created by statute and is, therefore, placed within legislative control.[1] As stated in an Illinois decision[2]: The statutes prescribe the exact conditions under which a will is admitted to probate and no court has the power to dispense with any of these prescribed conditions and to substitute something different on the basis of inherent, natural constitutional or other property rights.

"Whether a document is a will or not depends on the intent of the maker. In the absence of testamentary intent there can be no will. On the other hand a will cannot be established by merely proving an intent to make one. The first and foremost rule in regard to a will is to ascertain the intent of the testator and give it effect. If, however, the testator attempts to effect through his last will and testament what the law forbids, or to make a disposition contrary to public policy, no matter how clear his intent, his will must yield to the rules of law that will not permit his intent to be accomplished."[3] The essential requirements for a valid will have already been outlined on page 36, so that we simply refer thereto for these points.

We must distinguish in this connection between testamentary power and testamentary capacity, as one may have capacity but not power to make a valid will. Testamentary power is a right conferred by statute and is largely dependent upon age limitations. As Singer and Krohn state: "The rule is quite different in the case of real estate from that which obtains with reference to personal property. It has been quite generally held in both England and this country, in the absence of specific statutes to the contrary, that a male infant over fourteen years of age and a female infant over twelve years have power to dispose of personal property by will. If in the same will an individual over fourteen years of age made a properly attested will disposing of both real estate and personal property it has been held valid as to personal property. In many states, because of specific legislation, a legal infant cannot make a valid will under any circumstances. In some jurisdictions women at eighteen are allowed to make wills while that power is not conferred upon men until they are twenty-one."[4] Testamentary capacity has reference to the mental ability of the person making the will and is affected by the law only in so far as the court is the judge of this mental capacity to make a will, the insanity of the person involved being a question of fact. This capacity need not be of the highest order and relates solely to the questions involved in the making of a will. The points involved here are, as outlined on page 37 as follows: There must be an understanding of the fact that a will is being made; the testator must have sufficient memory to know the nature and general extent of his property; he must know his heirs and those bound to him by ties of blood; and he must be able to keep these facts in mind long enough to form a rational judgment in relation to the disposal of his property. The actual legal test of testamentary capacity is whether the testator, at the time of making his will, had sufficient mentality to understand that he was making a will disposing of his property. "The law requires a less degree of capacity to make a will than is necessary to make contracts and transact business which involve a contest of reason, judgment and experience and the exercise of mental powers not at all necessary to the testamentary disposition of property."[1] The law does not require the testator to possess a knowledge of the exact extent and value of his property, as persons of large estates rarely know the exact extent of their property; nor is it necessary that he knows the number and names of all those bound to him by ties of blood or that he appreciates the respective deserts of all of these, or that he is able to hold *all* of these facts in mind while making his will, as the test is whether he actually had mental capacity sufficient to do this.[2]

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[1] See Lane *v.* Walker, 110 Calif. 387; United States *v.* Perkins, 163 U. S., 625.

[2] Hill *v.* Kehr, 228 Ill. 204.

[3] See *Insanity and Law*, by Singer and Krohn, 1924, p. 319.

[4] See Deane *v.* Littlefield, 18 Mass., 239; Holzman *v.* Wager, 114 Md. 322; Goodell *v.* Pike, 40 Vt., 319; Moore *v.* Moore, 23 Tex., 637.

With reference to the effect of delusions of the testator upon his capacity to make a will, the courts hold that these may exist with legal testamentary capacity, providing they are of such a nature as not to effect the testator's ability to make a proper will. If the delusion is so closely connected to the terms of the will as to show the effect of the delusion upon the content of the will, then the will may be held invalid. A delusion sufficient to invalidate a will must be one whose influence controls the mind of the testator and destroys his freedom of action.[3] "The rule is well established", says the Supreme Court of Alabama[4], "that where there is an insane delusion in regard to one who is an object of the testator's bounty, which causes him to make a will which he would not have made but for that delusion, such will cannot be sustained." Mere prejudice of the testator against a relative cannot be held as sufficient ground for invalidating a will unless this prejudice can be shown to be related to a delusion on the part of the testator.[5]

It is clear from the above that an insane person may make a valid will and that, although mentally unsound, he may be of sound and disposing mind, as required by law. "It is true", says the Supreme Court of Ohio, "that a man may be 'medically insane' and yet capable of making a valid will . . . It is not the law in Ohio that an adjudication of insanity, or the appointment of a guardian, or both, makes a prima facie case of testamentary incapacity and places the burden on the proponents of a will to show the sanity of the testator so far as testamentary capacity is concerned."[1] On the other hand, the Supreme Court of Alabama says,[2] "We think proof of the adjudication of insanity, and that the deceased was under the guardianship of the probate court when she executed the will was sufficient to place on the proponent the burden of establishing testamentary capacity when the will was made; but the adjudication is conclusive of insanity only at the time of the inquisition and not prior nor subsequent to that time." As evidence of insanity, the will itself may be considered in its bearing on the case. While the reasonableness and propriety of the contents of the will may be taken into consideration, yet an unjust will is not in itself evidence of an irrational act, for a testator possessed of mental capacity may make an unreasonable and unjust will and may even disinherit his children.[3] For these reasons it has been held that a jury has no right to reject a will because its provisions appear to be unjust. The unreasonableness and unnaturalness of a will, however, is a circumstance which the jury may consider with other facts in passing on the mental capacity of the testator.[4]

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[1] See Rowcliffe *v.* Belson, 261 Ill. 566.

[2] See Bundy *v.* McKnight, 48 Ind. 502; Holmes *v.* Campbell College, 87 Kan., 597.

[3] See Johnson *v.* Johnson, 105 Md., 81; Rodgers et al *v.* Fleming et al. (Texas), 295 S. W. R., 326; Also, 3 S. W. (2d), 77; Jenkins *v.* Trice (Va.), 147 S. E. 251.

[4] Batson et al. *v.* Batson et al. (Ala.), 117 So. 10.

[5] See Nicewander *v.* Nicewander, 151 Ill. 156; Also, In re Barlum's Estate (Mich.), 215 N. W. R., 299.

The question of *undue influence*, exerted upon a testator to force him to insert certain provisions in his will, often must be considered in admitting a will to probate. By undue influence the courts have reference to "any means employed upon and with the testator, which, under the circumstances and conditions by which he was surrounded, he could not well resist, and which controlled his volition and induced him to do what otherwise would not have been done."[5] If the testator is so far under the control of others as to exclude all individuality, all thought and all action, it points to both undue influence and mental incapacity.[6] The force used to accomplish the result need not be of a physical nature. "The means may be flattery, importunity, threats, superiority of will, mind, or character, or whatsoever art, human thought, ingenuity, or cunning may employ which would give dominion over the will of the testator to such an extent as to destroy his free agency or constrain him to do against his will what he is unable to refuse."[7] While old age, physical weakness or infirmity or mental infirmities are not of themselves inconsistent with testamentary capacity and do not invalidate a will,[8] yet if these conditions have brought about some mental impairment, it is necessary to determine just how far such mental disturbance affects the testator's capacity to appreciate the nature of his acts. If these weaknesses, however, are combined with undue influence, they may be sufficient to warrant a refusal to probate the will. "Where there not only is, on the part of the testator, age, infirmity, and disease, but such advantage has been taken of his condition that the execution of will or codicils may well be ascribed to necessity and compulsion rather than a voluntary disposition, they cannot stand, and must be refused probate."[1] Such influence as will invalidate a will must be shown to have been exercised at or before the execution of the will and in direct relation to the will. It is not regarded as undue influence for a prospective beneficiary to attempt to persuade a testator to make a will, provided no effort is made to influence the volition of the testator as to the terms of the will, nor will undue influence be held if the possible beneficiaries request a third person to induce a testator to make a will, nothing being said as to its contents.

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[1] Kennedy *v.* Walcutt (Ohio), 161 N. E. 336.

[2] Houston *v.* Grigsby (Ala.), 116 So. 686.

[3] See Bradley *v.* Palmer, 193 Ill. 15; In re Finn's Estate, 22 N. Y. Supp., 1066; Kevil *v.* Kevil, 65 Ky., 614; Addington *v.* Wilson, 5 Ind. 137; Snow *v.* Benton, 28 Ill. 306; In re Lawrence's Estate (Pa.) 132 Atl. R. 786.

[4] See Carnahan *v.* Hamilton, 265 Ill., 508.

[5] See Chappell *v.* Trent, 90 Va., 849.

[6] See Messner *v.* Elliott, 184 Pa. St., 41.

[7] See "Mental Unsoundness" by Becker and Boston in *Medical Jurisprudence, Legal Medicine and Toxicology* by Witthaus and Becker, 1909, **3,** 415.

[8] See McCannon *v.* McCannon et al. (Texas), 2 S. W. (2d), 942.

LEGAL DETERMINATION OF INSANITY

By this we have reference to the procedure to be followed in adjudging a person insane. As we have seen, when an individual shows such an abnormal activity of his mental powers that his conduct becomes changed in relation to his surroundings and with reference to the rights and privileges of others, the case becomes a problem that must interest the courts and administrators of the laws, in order to protect both the individual and others from actual harm that might arise from acts committed by the one mentally disturbed. The exact method of procedure to be followed in determining the point of insanity is not by any means uniform, but, on the contrary, quite divergent and conflicting in the different states. It is important that the proceeding, called an inquisition, should be followed exactly according to the statute of the state in which the inquiry is held. After the adjudgment of insanity on a writ *de lunatico inquirendo*, the process of commitment to a state or private institution varies again in the various states.[2]

Owing to the variability of the method of procedure we give, herewith, the summary of the steps to be taken in this process as outlined by Singer and Krohn.[3]

1. The Petition.—Filing of a sworn petition alleging insanity. This may be done by a relative, a friend or any citizen, depending on the laws of the particular state in which proceedings are initiated. It must be done in the particular court on which the statutes of the state confer jurisdiction; *e.g.*, county court (Illinois), superior court (California), probate court (Indiana), supreme court (New York), district court (Louisiana), town officers (Maine), or board of commissioners (Nebraska).

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[1] See Jones *v.* Simpson, 171 Mass. 474; Swenarton *v.* Hancock, 9 Abb. N. C. 326.

[2] See "Summaries of State Laws Relating to the Insane" by Hamilton and Haber, in *Legal Medicine and Toxicology*, by Peterson, Haines & Webster, 1923, I, 718.

[3] *Insanity and Law*, 1924, p. 228.

2. Certificate.—A physician's certificate setting forth the results of an examination made within certain time limits prior to the hearing.

3. Notice.—Legal notice to the alleged insane person. What constitutes a legal notice to the respondent in such an inquiry is defined by the laws of the several states. In some states, notice to near relatives and others is also required by statute.

4. Hearing.—Hearing of evidence as to the alleged insanity of the respondent, at which hearing he, the person alleged to be insane, must be present unless the judge presiding at the hearing holds, with the statute of that particular state, that the health of the respondent would be jeopardized by his presence at the inquiry.

5. Before Whom Held.—The hearing may be before a jury (of six, twelve, or twenty-three fellow citizens) or before a commission (usually of physicians, two in number). In Illinois the lunacy hearing may be in open court, in chambers, at the home of the respondent or in a hospital where he may be a patient.

6. Verdict.—A verdict or return must be brought in by the jury or commission. Such verdict or return must be worded in the language of the statute conferring the jurisdiction. It is essential that the verdict shall define, substantially in accordance with the statutory definition, the disability with which the person involved is found to be affected. In some states the verdict or return must state of what the lunatic's estate consists. The verdict may be set aside by the court and a new hearing may be ordered. In some states, on the granting of a new trial, the inquisition may be changed from a hearing before a commission to a hearing before a jury.

7. Judgment on the Verdict.—By this the person found insane is committed to the care and custody of an institution (usually a state or county hospital for the insane, though in some states a commitment may be to a private sanitarium). In some states, he may be committed to the care and custody of an individual.

8. Transportation.—Transportation of the insane person to the institution to which he has been committed by the court. Funds for such transportation as well as the cost of maintenance of the patient at the institution are provided for by the laws of the several states.

Once adjudged insane, the status of the individual remains fixed until it is voided or revoked by law. Should the individual recover his sanity, he may petition the court for a writ of *supersedeas* to set aside the finding of the commission in lunacy. At any time during his sojourn in the asylum, a person adjudged insane may apply for a writ of *habeas corpus*, which, if granted, brings on an inquiry as to the sanity of the individual, or may secure a *mandamus* for a writ of discharge. After an individual is committed to a hospital for the insane, he may, if the authorities consider that he has been restored to sanity, be discharged by the superintendent of the hospital, by the hospital board of trustees on recommendation of the superintendent, by a special board of control, or by whatever statutory means are laid down in the various states. In such cases the court originally making the commitment to the hospital is notified by the hospital authorities of the discharge. When a person, who has been adjudged insane, recovers, the proper relief from the original findings of the commission is obtained only by application to the court exercising original jurisdiction, which court will void or revoke the original status on proper proof of return to sanity.

PART II

TOXICOLOGY

CHAPTER XVI

GENERAL PRINCIPLES OF TOXICOLOGY

Toxicology is the science of poisons, their origin, their properties, their action on the system, the treatment of their harmful effects, and the methods of their detection by chemical or other means. The medical practitioner usually concerns himself only with the recognition, prevention and cure of cases of poisoning, so that such phases of the subject may be spoken of as *medical toxicology*, in contradistinction to *forensic toxicology*, which is especially associated with the detection of poisons by chemical or other means in cases in which there may be criminal intent to do harm. While the physician usually has little to do with the legal phases of the subject, the forensic toxicologist must be familiar with all branches of the subject, so that his testimony may assume the broad aspects which are so important in any legal investigation.

It is a difficult matter to define what we mean by a poison, as it must be understood that there is no specific group of substances to which such a name applies. Many factors must be considered in deciding whether or not a substance is to be regarded as a poison in any specific instance. There is no substance known that is inherently a poison, that is that acts in a harmful manner under all circumstances and with all doses. However, it is impossible to set an arbitrary figure as to the amount of a substance which will produce toxic effects, as such action varies widely with different bodies and with the form in which the same substance may be administered. As Witthaus remarks: "It is with the poisonous quality, not with the thing which exhibits it, that we have to deal." Many of our best known and most widely used medicines may show toxic actions if given in large doses, while, on the other hand, most of our recognized poisons show therapeutic activity if given in small doses. For this reason we cannot sharply distinguish between a medicine, on the one hand, and a poison, on the other, without considering the question of the dosage of the particular drug used and certain other factors of which we shall speak below. Although we must have some knowledge as to the amount of any specific drug that will produce toxic symptoms, yet there can not be any arbitrary figure set down as the dosage which makes substances poisonous as differentiated from those that are non-poisonous. Each drug must be considered by itself and, hence, any definition of a poison in general cannot include the quantity necessary to determine this general action. When a specific drug is under discussion, it is perfectly proper to ask whether a certain dosage of this drug is or is not a poisonous one, but an answer to this question must refer only to the drug involved and to no other. Neither is a medical expert justified in answering a question, as to whether any specific drug, as strychnine for instance, is a poison, by the categorical "yes", as the answer must include a presumption of a certain dosage before strychnine may be regarded as a poison. Herter has said that "there is no soluble substance known that does not possess toxic properties when given in sufficiently large doses". Further, experimental proof has been forthcoming that pure water in excessive amount may produce severe poisoning and death.[1]

We believe that the most stisfactory definition of a poison advanced is that of Taylor as modified by Haines as follows: "*A poison is a substance which, when absorbed into the blood, is capable of seriously affecting health or of destroying life, and this as its usual effect upon the healthy body.*"[2] It will be observed that this definition excludes those articles, such as pounded glass, needles, etc., which produce their effects in a mechanical way only, as well as those substances which exert a local action on the external surface of the body or are not largely absorbed from the stomach and bowels and, as a result, exert their action mainly on the part to which they are applied. While strictly speaking we, therefore, exclude the class of bodies known as corrosives, yet in almost all cases there is some absorption of these corrosive bodies and some disturbance in the acid-base equilibrium of the system, so that harmful systemic effects may follow their administration. The corrosives do, without doubt, produce death in many cases by their marked action on the tissues, but certainly their external application would be definitely excluded by our definition, although some writers, as Guy and Ferrier, Mann, and Sollmann, include the external application of drugs in their conception of a poison. In a recent case in Nebraska[3], in which the accused was convicted of mayhem committed by the throwing of sulphuric acid, the Supreme Court gave the following definition of a poison, which covers the corrosives: "Poison may well be defined as any substance which when introduced into the system, either directly or by absorption, produces violent morbid or fatal changes or which destroys living tissue with which it comes in contact." As the law is chiefly concerned with the responsibility of a person for administering a poison, the question of definition and of mode of action is one largely left to the medical witnesses, the law being more involved with the proof that the substance criminally administered was actually the cause of the injury or death. For this reason the statutes make use of such expressions as "the administration of a poison or of other noxious or destructive thing", so that whatever may be the definition of a poison, it is certain to come under one of these headings.

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[1] See Rowntree, Arch. Int. Med., 1923, **32,** 157; Underhill and Sallick, Jour. Biol. Chem. 1925, **63,** 61; Babcock, Med. Jour. and Rec., 1925, **121,** 469.

[2] See *On Poisons* by Taylor, 1875, p. 18; "General Principles of Toxicology" by Haines in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, 2, 18.

[3] Hiller *v.* State (Neb.), 218 N. W. 386.

CONDITIONS MODIFYING THE ACTION OF POISONS

The effects of poisons on the system are not infrequently markedly influenced by a number of conditions, which relate (*a*) to the poison and the manner of its administration, and (*b*) to the individual to whom the poison is given.

1. Form of the Poison.—That the physical state of a substance will decidedly modify its action as a poison is clear, when we remember that no substance can act as a poison which is completely insoluble, as it cannot be absorbed into the blood. On the other hand, it follows that the more readily soluble a substance, the more easily it will be absorbed and exert its untoward effects. This point of insolubility is taken advantage of in the treatment of poisoning by antidotes which form insoluble substances with the poison in question. If, as our definition states, a substance must be absorbed and taken up by the blood before it can act as a true poison, it is clear that the most rapidly acting poisons are those in a gaseous state, following which come those in liquid form or solution, and lastly the solid types. The point involved here is merely related to the speed of action, as the general symptomatology will be much the same from the drug provided it is soluble, although in some cases quite irregular or even unexpected results may follow the administration of the drug in solid form, as in pills or capsules. As a rule dilution of a poison with water favors its more rapid absorption and may, for this reason, intensify its action; while with the corrosives dilution diminishes the activity. A further point to be considered is the condition of the stomach, as regards the presence or absence of food. It is well established that the action of a poison is slower and often less severe, if it be taken when the stomach is full of food, as absorption is retarded; while, if the stomach be relatively empty, absorption and toxic effect appear much more promptly.

2. Avenues of Absorption.—As stated above the rapidity of absorption depends largely on the physical state of the poison. While the effects of a poison, by whatever channel it may be absorbed, are ordinarily the same, yet there may be quantitative differences due to variations in rapidity of absorption.[1] The symptoms appear much more rapidly when the poison is administered by inhalation, by intravenous injection, by intramuscluar or hypodermic injection, than when it is given by mouth, but the ultimate effects of the drug given by mouth will be almost identical to those noted when it is given by the other routes. However, in some cases, substances given by mouth are practically inert, while extremely active if given by intravenous or intramuscular injection, as, for instance, snake venom, curare, and ricin; while hydrogen sulphide and chloroform, both of which are extremely active when taken by inhalation, show little or no effect when given by mouth.

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[1] See Kolmer, Jour. Pharm. and Exp. Therap., 1921, **17**, 433.

3. Quantity of Poison Administered.—The fatal effects of a poison depend more on the quantity absorbed in a given time than upon the absolute amount administered. While it is generally true that the larger the dose the more rapid and more severe the effects, yet this is not always the case, as such poisons as arsenic and antimony, when given in very large quantity, may produce such marked irritation of the gastric mucosa that the resulting excessive vomiting may almost completely eliminate the poison, although frequently in such cases there is enough absorbed to produce some general toxic symptoms. The writer recalls the case of Mrs. Vermilya, who had poisoned several persons with arsenic and had been finally suspected and apprehended. While she was under the supervision of a police matron, she herself took a very large amount of Rough on Rats with suicidal intent. Vomiting began very soon, the first vomitus being lost as no suspicion was attached to her at that time. However, the several later specimens of vomitus were preserved for examination and were found to contain three heaping tablespoonsful of the Rough on Rats. She recovered from the acute symptoms, but later developed the nervous symptoms of arsenical poisoning, but did not die from the effects of this enormous dose.

Even with the most active poisons, there is a limit below which they are inert, while slightly larger doses are of remedial value, while still larger doses show toxic or fatal effects. Just what we are to regard as the lethal dose of a poison is a difficult matter to say. With animals the minimum lethal dose may be readily determined as the smallest quantity per kilo body weight which will cause the death of the animal. However, with the human no such method of experimentation is possible and the adaptation of the fatal doses for animals to man may give rise to serious error owing to the variability of susceptibility of different animals to the different drugs. We are, therefore, forced to state that the fatal dose of a certain poison for man is the smallest dose that has been known to have caused death. Obviously this leads to serious error as the exact amount of a poison taken in a criminal or suicidal case is rarely known and the analyst is unable to say from his examination just how much was taken, as his results indicate simply the amount of the poison found by him and have no reference to the amount that may have been lost by the various channels of elimination. A further difficulty arises in determining how much of a certain poison was actually absorbed after it was administered. Obviously, the analyst does not examine the entire body, so that he is not able to give accurate data as to this point. The poison found in the stomach is, in most cases, to be regarded as that part that has had little or nothing to do with the poisoning, as it has not as yet undergone absorption. For this reason, it must be said that, although there can be little doubt that the quantity of any poison capable of causing death under given conditions has a certain minimum limit, yet just what this quantity is must be regarded as more or less unknown. When we rely upon reports of cases found in the literature, we must remember that in few of these cases is the exact amount of the poison taken definitely known. Where death has resulted from an intake of a known amount, then we are justified in stating that such an amount has proved fatal, but whether it would do so in other cases, we are not in a position to say with certainty. As Witthaus states: "The dose must be small and known with accuracy, it must have proven fatal under conditions which exclude other causes of death, and no part of it can have been removed by vomiting or by treatment."

A further point to be considered in connection with the quantity of poison administered is that, while one dose may prove fatal from acute poisoning, small and repeated doses may lead to a chronic type of poisoning, in which the symptoms are quite distinct from those of the acute stage. In other words, the quantity administered may determine the type of poisoning in any given case.

With reference to the factors which modify the action of poisons, those relating to the individual to whom the poison is administered are (1) Age, (2) Idiosyncrasy, (3) Habit, (4) Tolerance, and (5) Physical Condition of the Subject.

1. Age.—It is well known that the dosage of medicinal agents is modified according to the relative age of the patient, in the sense that children must be given relatively smaller doses than the adult. For the same reason, we find that age modifies the susceptibility to poisons. While it is generally the case that the younger the person, the greater the susceptibility to the action of a poison, yet we find that such is not always the case. Thus, children appear to be more tolerant of belladonna, calomel and strychnine than are adults; while, on the other hand, opium and its derivatives, as well as narcotics in general, often show extremely severe reactions in children. As is the case in children, so it is with the other extreme of life, namely in old age, when it is not unusual to find extreme reactions from doses of drugs or poisons, which would be much less active in younger adults.

2. Idiosyncrasy.—It may be observed by almost any practitioner that some of their patients show a peculiar or unusual reaction to certain drugs, some of them even to such an extent that serious disturbance or even death may result. For this reason, the possibility of this unexplained sensitiveness should always be remembered in investigating any particular case of poisoning. It is not always that this idiosyncrasy is manifested only towards poisons, as some individuals show such untoward reactions to such comparatively harmless drugs as quinine. Of the more common poisons, which may be associated with such unusual reactions in some individuals, we find, antipyrine, morphine, calomel, and arsenic. It is probably due to this cause that we occasionally meet with cases of poisoning from doses of drugs, which should be merely remedial; while, on the other hand, we not infrequently see cases in which morphine fails to exert its soothing action but produces instead a wakeful, restless state, which may be accompanied by convulsions. It should be mentioned in this connection, that some individuals show such peculiarities after taking many common foods, such as shell-fish, eggs, certain meats, strawberries, apples, etc.

3. Habit.—Following the continued use of many of the common poisons, especially if the beginning dosage be small and gradually increased, most individuals may become accustomed to them to such an extent that really enormous doses may be taken with more or less impunity. Such is the case with the morphine habitue. Further, individuals accustom themselves to the intake of arsenic, as reported from Styria, to such an extent that doses of arsenic may be habitually taken by these so-called arsenic eaters without causing any signs of poisoning, while the same dose taken by one unaccustomed to it would probably result fatally. In this connection it should be stated that Schwartze believes that this tolerance for arsenic is closely related to the physical condition of the arsenic taken, the smaller the particles or the more finely powdered the drug, the quicker its absorption and resultant toxic effects. Other examples of such drugs as the above are cocaine and strychnine, both of which may be given in increased doses without causing unusual symptoms.

It is to be recalled, however, that this tolerance formed by habit is only a relative one, as severe symptoms and even death may follow doses which exceed the accustomed limit only slightly, as may be noted in the death of many morphine habitues, as well as of the cocaine users, when the amount taken has gone beyond the limit to which they were habituated.

4. Tolerance.—Occasionally individuals are observed, who show a natural resistance toward the action of poisons, which has not been acquired by habituation as in the cases above mentioned. No satisfactory explanation of this condition has been forthcoming, but that it exists is well-established. Some persons, who are entirely unaccustomed to its use, are capable of taking such large doses as 1 grain of morphine sulphate without manifesting any apparent effect.

5. Physical Condition of the Subject.—It is to be expected that a person in full vigor will tolerate drugs and poisons better than one who is suffering from some disease. For this reason, we should expect to find that the action of poisons may be modified by disease, in some cases the effect being increased while in others it is greatly diminished. Of special importance in this regard are those conditions which affect the rate of absorption from the intestines as well as those in which elimination is retarded. Thus, renal disease, especially those types in which elimination is greatly reduced, increases the susceptibility of the individual, owing to the accumulation of the poison in the blood and tissues, a dose that would ordinarily not produce untoward effects often leading to very serious consequences. In those diseases, such as peritonitis, renal calculus, and others, associated with intense pain, morphine is remarkably well tolerated; while in inflammatory conditions of the brain and nervous system an increased susceptibility may be observed. In mental disturbances the narcotics may show very little influence in quieting the individuals.

FATE OF POISON INTRODUCED INTO BODY

According to our definition of a poison, such a substance must be absorbed into the blood before it can exert its toxic effect. After its absorption some of the poison is more or less rapidly excreted, principally through the urine, saliva, bile, and perspiration, while certain of the poisonous substances are either only slightly absorbed or are reexcreted into the stomach and bowels and are eliminated in the feces. Lead, for instance, is more largely excreted by way of the feces than by the urine. It should not be supposed that all poisons are eliminated with the same rapidity, as much variation is shown in this respect. While a portion of all poisons is eliminated by the various excretions, another portion is retained by the tissues of the body, the distribution being more or less general throughout the body, but some organs retaining more than others. As a rule, the liver is the organ which retains the most of the poisons held in the system, so that in toxicological examinations this organ is probably the most important one for general examination, although some poisons, especially those producing their effects by inhalation, are retained in the liver to a very slight extent if at all, the lungs being the principal organ of excretion.

It is probable that the retention of a poison in the tissues is due to the formation of some chemical compound, the exact nature of which is unknown. In this combined state its toxic effect is relatively slight, so that such combinations may be regarded as the attempt of the system to detoxicate a poison introduced. It seems to be well established that those poisons, that do not have any special chemical action upon the blood or do not form insoluble compounds with the tissue elements, are quite rapidly removed from the body after absorption. For this reason we find that, if elimination keeps pace with absorption, practically no symptoms of poisoning occur, while, if the poison is more rapidly absorbed than it is eliminated, it must accumulate in the blood and be deposited in the tissues. For this reason we are justified in stating that the lethal action of a poison is a function of the quantity absorbed rather than the quantity administered, that is the accumulation of a poison in the blood and tissues is necessary before symptoms of poisoning will occur. Where the poison is given in a large dose and much of it is absorbed, the system may be so overwhelmed with the poison that the toxic action is rapid and death may be sudden. However, if the drug is slowly absorbed, the accumulation is not so great and, in consequence, the appearance of symptoms is slower and the fatal result may be much delayed. In the case of the frequent administration of small doses of a poison, the chronic type of poisoning is produced, so that the symptomatology will vary much from that of the acute type owing to the fact that there is not sufficient of the poison in the blood at any one period to produce the usual acute symptoms, and, also, that some of the drug has been eliminated. However, in such cases, we find that some of the drug is retained so that, when a fresh supply is added, the symptoms may be somewhat exaggerated as a result of the so-called "cumulative" action of the poison. Chronic poisoning with lead, arsenic, etc., may not prove fatal for some time, but sooner or later the system will be so undermined by the constant action of these small doses that death will result.

The diffusion of the poison throughout the body by means of the blood is an established fact, but, as stated above, it must not be assumed that this distribution is equal in all organs. Thus, with arsenic, we find a large amount in the liver, somewhat less in the kidneys, heart, and spleen, while, in cases in which very little has been found in these organs, the bones have been shown to yield quite appreciable amounts. Further, while elimination may begin very soon after absorption of a poison, the rate of such elimination varies with the different poisons, so that one can not state an exactly definite time as to just when a certain dosage of a poison will be eliminated from the system, nor can he state exactly how long after administration of a poison, the liver, for instance, will have received its maximum saturation with the poison. There are many variables that enter into these questions of relative absorption, deposition and elimination of a poison, so that each case is largely a law unto itself, although there are certain general deductions that may be warranted.

DIAGNOSIS OF POISONING

It is clear that an early diagnosis of poisoning is greatly to be desired, in order that prompt and proper treatment may be instituted. However, this is usually very difficult to attain and is, in fact, often impossible during life. There are probably very few poisons, with the possible exception of the corrosives and occasionally strychnine, which give sufficiently characteristic symptoms to warrant a diagnosis of poisoning as distinguished from certain diseases with which they might be confused. Often the presence of burns or signs of corrosion on the mouth or tongue may lead to the conclusion that a corrosive has been taken, while the odor of the breath may lead to the detection that such a poison as carbolic acid, chloroform, crude opium, or cyanides has been administered. If the vomitus be obtained, phosphorus may be assumed by the luminosity in the dark, and particles of white crystalline particles may lead to the finding of arsenic, while, not infrequently seeds or other portions of a plant may give evidence of the taking of some active drug. Careful consideration of such findings may be most important. This association of symptoms with both disease and poisonings has been so well outlined by Haines[1] that we quote him directly in this connection.

"**The diseases simulating poisoning** are many, those resembling *irritant poisoning* being chiefly, cholera, cholera morbus, acute indigestion, ulceration of the stomach or duodenum, gastritis, gastro-enteritis, peritonitis, appendicitis, hepatic and possibly renal colic, and intestinal obstruction; while those whose symptoms resemble *poisoning by neurotics* are, among others, hysteria, cerebral hemorrhage and thrombosis, epilepsy, the convulsions of certain brain diseases, tetanus, inflammation of the brain and its coverings, uremia, and organic heart disease.

"As an aid to diagnosis we give below lists containing the commoner poisons and the diseases which produce the stated symptoms as their usual and expected effect; but it should be remembered that unusual and unexpected symptoms may follow the administration of almost any poison, and the same deviation may be shown by the symptoms of disease.

"**Vomiting** (frequently associated with **purging** and abdominal **pain**).—*Poisons.*—Arsenic, antimony, aconite, corrosive acids and alkalies, barium, colchicum, cantharides, digitalis, copper, iodine, mercury, phosphorus, phenols, wood alcohol, veratrum, zinc, poisonous foods. *Diseases.*—Gastritis, gastro-enteritis, gastric and duodenal ulcer, cholera, cholera morbus, cholera infantum, uremia, acidosis, onset of many acute infectious diseases, the early stages of pregnancy, brain tumor.

"**Convulsions.**—*Poisons.*—Aspidium, brucine, camphor, cyanides, santonin, strychnine. *Diseases.*—Uremia, puerperal eclampsia, tetanus, epilepsy, many acute disturbances of the cerebrospinal system, especially meningitis.

"**Coma.**—*Poisons.*—Opium and most of its derivatives, hydrated chloral, sulphonal, trional, veronal, paraldehyde, chloroform, cyanides, carbon monoxide, carbon dioxide, atropine, hyoscine, the various alcohols and phenols. *Diseases.*—Uremia, puerperal eclampsia, acidosis, cerebral hemorrhage, cerebral thrombosis and embolism, brain injury, epilepsy and other brain diseases.

"**Dilatation of Pupil.**—*Poisons.*—Belladonna, stramonium, hyoscyamus, scopola, and their derivatives, gelsemium, cocaine, nicotine. *Diseases.*—Certain nervous diseases causing optic atrophy, sympathetic irritation, or weakness of oculomotor nerve.

"**Contraction of Pupil.**—*Poisons.*—Opium and its derivatives, physostigma and its derivatives, pilocarpine, muscarine. *Diseases.*—Certain nervous diseases, such as tabes.

"**General and Partial Paralysis.**—*Poisons.*—Cyanides, carbon monoxide, carbon dioxide, botulism. *Diseases.*—Apoplexy, brain tumor, meningitis.

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[1] "General Principles of Toxicology", in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 24.

"**Slow Respiration.**—*Poisons.*—Opium and its derivatives, carbon monoxide. *Diseases.*—Uremia, compression of brain as from hemorrhage.

"**Rapid Respiration.**—*Poisons.*—Atropine group, cocaine, carbon dioxide. *Diseases.*—Acute respiratory diseases, lesions of the medulla oblongata, hysteria.

"**Delirium.**—*Poisons.*—Atropine group, cannabis indica, cocaine. *Diseases.*—Epilepsy, insanity, delirium tremens, organic brain diseases such as meningitis, visceral diseases such as nephritis.

"**Dyspnea.**—*Poisons.*—Strychnine (during the convulsions), cyanides, carbon monoxide. *Diseases.*—Diseases of cardiac and respiratory system, lesions of medulla oblongata and of vagus nerves.

"**Cyanosis.**—*Poisons.*—Nitrobenzene, aniline, acetanilide, opium. *Diseases.*—Same as under dyspnea, prolonged convulsions from any cause producing cardiac dilatation."

Where there are no direct indications pointing to the administration or taking of a poison, the physician must be largely guided by the symptoms shown, but these, as we have seen above, may be anything but clear. The sudden appearance of the symptoms in one, who has previously been in good health, is very suggestive of poisoning, as most diseases do not produce their symptoms suddenly, although apoplexy, valvular lesions of the heart, acute obstruction of the bowels, etc., may suddenly manifest themselves and prove rapidly fatal. Further, the symptoms of poisoning usually make their appearance soon after the victim has ingested food, drink or medicines, so that the physician should always be suspicious of such an onset of the trouble. There are, however, some diseases of the gastro-intestinal tract that are much aggravated by taking of food or drink, so that it is not by any means always certain that the cause of the untoward symptoms is poisoning. However, if a number of persons, partaking of the same food, show similar symptoms, one is usually justified in assuming that some sort of poisoning is at the bottom of the attacks. Yet, it is possible for several individuals to partake of the same food and only one show marked symptoms, as some of the persons may have a tolerance for the poison, if any be present, while, on the other hand, the portion served to only one person may have been treated with the poison in question.

It will thus be seen that it is seldom possible to make an absolute diagnosis of poisoning during life, unless, perhaps, one has access to the vomitus or urine of the victim, when a chemical examination may reveal the cause of the symptoms. However, such analyses may require too long a time to be of any value in the treatment of the case.

In the case of chronic poisoning, the symptoms are usually so indefinite and obscure that a diagnosis is ordinarily more difficult than in the case of the acute poisonings. Of course, if there is any history of exposure to possible poisons, as in various industrial pursuits, the physician may be suspicious and use various means of clinical and chemical nature to solve his problem.

TREATMENT OF POISONING

It is true that specific treatment is dependent upon the particular poison administered, but in many cases, at least, the special poison involved is unknown, so that general methods should be used which are applicable to all poisons. These general procedures are as follows: (1) Removal of the poison from the stomach; (2) administration of antidotes; (3) elimination of the poison absorbed; and (4) symptomatic treatment.

1. Removal of the Poison from the Stomach.—Most cases of poisoning occur as a result of oral administration of the poison, although, of course, some arise after introduction by means of inhalation, hypodermic or intravenous injection, or even as a consequence of rectal or vaginal introduction of the poison. Unless the poison has been introduced by the oral route, there is little hope of accomplishing much by attempts to remove poison from the stomach, although such drugs as morphine and arsenic are excreted into the stomach after administration by parenteral methods, so that in such cases something may be gained by washing out the stomach in order to prevent reabsorption.

If it is decided to attempt to remove the contents of the stomach, and this is almost always the thing to do promptly, except possibly in the case of strychnine poisoning where convulsions may be brought on by such attempts, or of corrosive poisoning when there may be danger of causing perforation, probably the best means is by the use of the stomach tube, as this ensures more prompt and thorough emptying of the stomach, is less depressing, as a rule, to the patient, and permits of a simultaneous introduction of an antidote. The tube should be introduced to the mark found on it, that is to a distance of 45 to 50 cm. from the teeth, and a funnel should be placed in the outer end of the tube, through which is poured from ½ to 1 liter of tepid water, or this fluid may contain certain antidotes to be discussed later. Before the entire amount of water has flown out of the funnel, the tube is compressed with the fingers and the funnel removed. On now lowering the tube while still closed and then releasing the pressure, the contents of the stomach may be siphoned off into a clean vessel made ready for this purpose. This process should be repeated several times in order to insure more or less complete washing out of the stomach. Of course, if the stomach contains much food, particles of this may clog up the tube and prevent the removal of the contents, so that resort will have to be made to other means of emptying the stomach.

If the stomach tube seems impracticable, vomiting must be promoted by the use of emetics or by such measures as tickling the back part of the throat with the fingers or a feather. Probably the emetic of choice is apomorphine hydrochloride in a dose of 0.007 gm. (1/10 gr.) given hypodermically. This drug causes emesis by acting on the vomiting center in the medulla and acts rather promptly (five to ten minutes), but it must be remembered that in narcotic poisoning apomorphine may not act at all, owing to the depression of the vomiting center by these poisons. If an emetic is to be given by mouth, one may use a dessertspoonful of ground mustard stirred up in a small cup of tepid water, 1 to 1.5 grams of zinc sulphate, 0.3 to 1 gram of copper sulphate, repeated if necessary in 15 to 30 minutes. In irritant poisoning, the reflex vomiting set up by the poison is usually sufficient to accomplish all that emetics would do, so that it is inadvisable to administer further emetics as we wish to allay rather than to increase the gastric irritation in such cases. Here, one should resort to the washing out of the stomach rather than to administer emetics. If, however, vomiting is desired, this should be continued until the stomach is thoroughly cleansed and lavage should follow this in all cases, employing chemical antidotes in the wash water to neutralize any poison that may remain in the stomach. In corrosive poisoning, one is between Scylla and Charybdis in the matter of emptying the stomach, as the pressure on the walls of the stomach, exerted by the contraction of the diaphragm and abdominal muscles incident to the attempts at vomiting following the emetics, may rupture the weakened stomach walls, while the introduction of the stomach tube may cause perforation, although Hemmeter[1] believes it is better to allow the patient to take his chance of perforation rather than to leave the corrosive in the stomach. Possibly the better course would be to administer by the mouth a chemical antidote and leave the resulting neutralized poison in the stomach, as the effects of corrosives are usually immediate and the damage is done before we get a chance to do anything.

In all cases, if the stomach has been emptied, it is important that the material withdrawn or ejected be received in thoroughly clean vessels, in order that no outside contamination may be introduced. The evacuated material should be carefully inspected for gross evidence of possible poisons, as, for instance, white, slowly soluble grains of arsenic trioxide, seeds or other portions of poisonous plants, or for possible odors which may give a clue as to the poison. After such inspection the material should be carefully sealed up and preserved for later chemical examination, should legal proceedings follow.

2. Administration of Antidotes.—Antidotes act either physically or mechanically by enveloping the poison in some insoluble material or chemically by changing the composition of the poison, so that a sparingly or insoluble compound is formed, which is either inert or very slightly toxic. However, some of the chemical antidotes produce compounds which may be relatively soluble in the acid secretions of the stomach and, hence, may prove toxic should they remain there for any length of time. For this reason it is wise to combine the administration of the antidote with lavage, so that the new compound may be washed out as completely as possible, and fresh amounts of the antidote should again be given, followed up with another lavage. In this way the poison in the stomach is not only rendered inert but is removed.

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[1] *Diseases of the Stomach*, 2nd ed. 1900, p. 443.

Antidotes, which act mechanically, are of special value inasmuch as these are usually at hand and may be administered promptly before one may have time or opportunity to obtain the more specific chemical antidote. Such mechanically acting substances are fats and oils, milk, white of eggs, flour and very finely powdered charcoal. In the case of eggs or milk, the protein may combine with such poisons as mercury, forming an insoluble compound, while the charcoal is specially effective in absorbing the alkaloidal poisons, a property which has been shown to be possessed by fuller's earth. The fats and oils are doubly effective by retarding the absorption of the poisons and by protecting the mucous membrane from further irritant action of many of the poisons. However, these fats and oils, as also unskimmed milk, should not be used in poisoning by phosphorus, as they dissolve this poison and render it more active.

Chemical antidotes are such as may either form insoluble compounds with the poison or by acting chemically in such a way that the nature of the poison is changed and rendered temporarily, at least, inert. Thus, tannin produces insoluble compounds with most alkaloids, ferric hydroxide forms a compound very slightly soluble in water but more or less readily soluble in the gastric acids, while acids neutralize alkalies, and such oxidizing agents as potassium permanganate change morphine to oxydimorphine. In the use of chemical antidotes for the various poisons it must be remembered that many of these compounds are not absolutely harmless in themselves and many of them are relatively soluble in the acids of the stomach, so that lavage should be practiced following the administration of the antidote. The antidote chosen to combat a poison in the stomach should, of course, be one that is, *per se*, harmless or relatively so, in order that there may be no ill effects from this if an excess should be given.

The special antidotes, where such exist, will be given under the discussion of the specific poisons, but it may be well to mention here that, in alkaloidal poisoning, 15 drops of tincture of iodine in half a glass of water, tannic acid in the form of strong tea, and potassium permanganate, about 0.2 gram dissolved in a glass of water, are valuable agents. Occasionally, where there is no knowledge as to the type of poison that has been administered, a so-called "universal" antidote may be used in the hope that some portion of it may act favorably. A good example of this type of antidote consists of 2 parts of powdered charcoal, 1 part of tannic acid, and 1 part of magnesium oxide, giving a heaping teaspoonful of the mixture in water, frequently repeated if necessary.

There is a further class of antagonistic agents, which, strictly speaking, are not antidotes, but act in a manner antagonistic to that of specific poisons and may, therefore, be used to counteract their effects on the system. Such substances do not, of course, combine chemically with the poison in the stomach, but may be used hypodermically, if necessary, to counteract the systemic effects of certain poisons. Thus we find as physiologic antagonists atropine and pilocarpine, strychnine and nicotine, digitalis and aconite, chloral or chloroform to strychnine, caffeine to morphine, and, only partially, atropine to morphine. If such antagonists be used, in any specific case of poisoning, care should be taken to see to it that an excessive amount of the antagonist is not used as, otherwise, the poisoning may be changed to one caused by the introduction of the supposed physiologic antidote.

3. Elimination of the Poison.—As the poisons produce their harmful effects only after absorption and circulation in the blood, it follows that it is wise to attempt to increase elimination as much as possible, so that the further absorption of the poison may be somewhat compensated by the elimination of that formerly absorbed. Such measures are, however, rarely of much avail in the cases of acute poisoning, as our methods of elimination do not act quickly enough to enable elimination to keep pace with absorption. However, in the more chronic types of poisoning this increase in elimination is of much value.

The chief avenues of elimination are the kidneys, skin and bowels, the kidneys being the most important. Probably the best diuretic is pure water, given in copious amounts (4 to 8 liters or more daily). Of course, if the kidneys are involved in the changes occurring as a result of the action of the poison, the increased strain put upon them to eliminate this increased fluid may be harmful in itself. If there is no contra-indication, one may add to the water such diuretics as potassium acetate, caffeine, theobromine, etc., in the hope that elimination of the poison may be accelerated. If there is difficulty in voiding the urine, accumulation in the bladder should be prevented by catheterization. The skin should be kept active by heat and the bowels should be emptied by enemas or mild laxatives.

A further method of increasing elimination is by the hypodermic injection (hypodermoclysis) of physiologic salt solution. This solution may be approximated by dissolving a heaping teaspoonful of common salt in a quart of hot water. Usually about a liter of this solution is injected at a temperature of about 40°C., and this should be repeated several times daily. This method of administering fluid favors more rapid elimination through the kidneys than does the oral route. If the poison be one that acts with great rapidity, one may resort to the intravenous injection of physiologic salt solution or of Fischer's[1] solution. This method not only increases elimination through the kidneys, but may, also, stimulate a flagging heart and in this way act most beneficially.

4. Symptomatic Treatment.—The treatment of the symptoms arising from the taking of a poison should be started at once, as it is the systemic effect of the poisons, as manifested by the symptoms of the patient, that are the dangerous factors in any case of poisoning. The patient should be kept quietly in bed and not be disturbed by any more outsiders than is absolutely necessary. Artificial heat should be applied to prevent cooling of the body, and such general stimulants as inhalation of ammonia, administration of aromatic spirits of ammonia, and strychnine hypodermically should be employed. Pain should be controlled by appropriate anodynes; cardiac failure should be combated by strychnine, nitroglycerin, or digitalis; respiratory weakness by the general stimulants mentioned above, by flicking with wet towels, or, if the respiration be much embarrassed, by artificial respiration; coma prevented, if possible, by the use of strong coffee or administration of atropine; convulsions controlled by administration of chloroform by inhalation or chloral hydrate by mouth or per rectum. In cases of poisoning with gases, in which deficient oxygenation of the blood is a prominent symptom, inhalation of oxygen alone or, in such poisonings as that with carbon monoxide, oxygen mixed with small amounts of carbon dioxide, may prove very beneficial. Special methods of treatment will be given under the various poisons discussed later.

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[1] The composition of this solution is as follows: Crystallized sodium carbonate 10 gm., sodium chloride 14 gm. dissolved in 1000 cc. of distilled water and sterilized by boiling.

POSTMORTEM EXAMINATION

We shall not attempt to discuss the technic of making the necessary postmortem examinations in connection with cases of poisoning, but shall confine our remarks in this connection to certain special points involved. It should, perhaps, be remarked, that the postmortem investigation should be a very thorough one, in order that every precaution be observed to solve the question as to the cause of death of any particular case. It is of especial importance to know whether or not there are present natural causes of death, as such a point will necessarily arise in any legal investigation, and this can be settled only by a complete autopsy.[1]

While it is advisable that the autopsy be performed promptly and before embalming has taken place, yet it often happens that no suspicion as to possible poisoning arises until some time after burial has occurred, so that the body may have to be exhumed and examined under conditions which are far from satisfactory both as regards the pathological as well as the toxicological findings. It is, of course, clear that, if the body be embalmed with arsenical fluids, no importance can attach to the chemist's finding of arsenic in the body; further, if the embalming fluid be one containing formaldehyde, detection cf poisoning with the cyanides is practically prevented by the combination of the cyanide with the formaldehyde to form isonitrils, for which we have no characteristic tests. Putrefactive changes, if far advanced, may preclude the possibility of detecting many of the alkaloidal poisons.

As is the case with the symptoms produced by poisons, the pathological changes found in the tissues on autopsy are rarely conclusive. With the possible exception of the corrosives, no poison produces changes in the tissues which are not identical, for all practical purposes, with those that may be produced by disease. Hence, about all that the pathologist is able to state from his autopsy findings is that the changes noted are such as might occur from a certain poison or, at least, are compatible with the assumption that such a poison is the cause of the findings. "The chief value of a postmortem examination in a case of suspected poisoning, aside from securing organs for chemical analysis and other scientific investigations, lies (1) in determining whether such appearances are present as are usually produced by poisons, or at least are compatible with it, and (2) in disclosing the presence or absence of natural causes of death. In regard to the first of these points, it should be borne in mind, however, that the postmortem appearances produced by no poison are always the same, and sometimes, as before stated, even the most characteristic marks may be wholly absent; and concerning the second point it is scarcely necessary to state that death may occur from poison even though the person at the time was suffering from a serious or even necessarily fatal malady."

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[1] In this connection see "The Technic of Medicolegal Postmortem Examination" by Hektoen and LeCount, in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, 2, 78; or "Medicolegal Autopsies" by Loomis, in *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 1906, I, 833.

When an autopsy is to be performed in a suspected case of poisoning, it is wise to have the toxicologist, who is to make the chemical examination of the organs, present, if possible, in order that he may personally see to it that the specimens of tissue are properly handled and collected. However, this is rarely done, as at the time of the autopsy it may not have been decided what is to be done with the organs removed, so that it not infrequently happens that contaminations are introduced by carelessness on the part of those making the autopsy. While it seems to be frequently considered as sufficient to remove only the stomach for chemical examination in cases of poisoning, yet it should be remembered that the poison that is found in the stomach has not as yet taken an active part in the poisoning, as, for all intents and purposes, this poison is still outside the body, that is it has not, with very few exceptions, been absorbed and can not, therefore, act as a poison under our definition. Further, the stomach may show no poison owing to its elimination either by absorption or by vomiting, so that the results of examination of this organ alone would be negative, when quite appreciable amounts might have been found in other organs. In all cases, the toxicologist should insist on having a large part of the liver (of which he should know the total weight), both kidneys, a part of the intestines, and, in some cases, he may require the brain and spinal cord, or, if death from chloroform or ether is suspected, the lungs.

As soon as it is examined by the pathologist and specimens obtained by him for his microscopic investigations, each organ should be placed in a thoroughly clean wide-mouthed glass jar with glass top instead of the usual metal screw-cap. If the chemist collects his own specimens, he will, of course, see to it that everything that comes in contact with the organs, which he is to examine, is known by him to be clean; but, if, as usually happens, the one who performs the postmortem examination places the organs in the vessels, unwitting mistakes may lead to contamination, of which the chemist is of course unconscious and may, therefore, make a report of the presence of substances which have had nothing to do with the actual poisoning. As soon as the organs are placed in the jars, these should be carefully sealed in such a way that no tampering with the contents can occur without being easily discovered. It is preferable to add no preservative to the organs, but, rather, to transport them as rapidly as possible to the toxicologist, who can then do with them as he sees fit. If, for any reason, it seems desirable or necessary that a preservative be added either pure grain alcohol or 10 per cent. formalin may be used (except that the latter should not be used if cyanide or phenol poisoning is suspected). If either of these preservatives have been used, several ounces of the same fluid as that added to the tissues should be sent to the toxicologist along with the tissues, in order that he may be able to examine this for the presence of any poison that he may find in the tissues.

It is, perhaps, unnecessary to mention that the identity of organs examined in a case of poisoning be established, beyond any doubt, as those removed from a certain body. If the chemist, himself, collects the specimens at the time of the autopsy, he, of course, is in a position to testify as to their identity. However, when such organs are to be transported to the chemist, the greatest care must be exercised in order to prevent any possibility of a question arising as to the source of the organs examined. The best way to insure this is to have some representative of the coroner or the state's attorney carry the organs directly to the chemist and turn them over to him personally. If this does not seem feasible, then the well-packed, carefully sealed specimens may be sent to the toxicologist by insured express with the request that the person to whom directed personally sign the receipt. In this way a direct relation between the sender and receiver is established so that the identity of the organs may be established, should any question arise later. On receipt of the specimens, the toxicologist should make careful notes as to the method by which the specimens were sent to him, from whom received, the time received, and the place where they were received. He should carefully describe the package received by him, should note the sort of wrappings, the nature of the cord binding the package, the type of container in which the specimens were sent, and the presence or absence of special seals and, especially, as to whether there was any evidence that the seals had been tampered with. This will all have to come out in the trial and the person from whom he received the package will probably testify as to the nature of the package sent or brought by him. If there should be any discrepancy in the two descriptions, the opposing attorney will be quick to take advantage of the possibility of doubt that the specimens received were not those sent.

CHEMICAL ANALYSIS

As we have seen, it is only rarely that a case can be positively diagnosed as one of poisoning from the symptoms and just as rarely does the postmortem examination establish the cause of death as due to poisoning. For this reason resort must be made to the chemical examination of the viscera in the hope that a definite poison may be isolated in such a state of purity as will permit of its identification and quantitative estimation. It should be stated, perhaps, that it is not absolutely necessary that a chemical analysis of the viscera be made or that a poison be found in such examinations in order to prove that death resulted from poison, as the circumstantial evidence may be such as point to death from such a cause, especially when the symptoms and autopsy findings are compatible with poisoning. All that is required legally is that there should be convincing proof of death from poisoning. The finding of a poison in the body does not prove, necessarily, that death was caused by it, nor is the fact that no poison is found evidence that poison did not cause the death. It is well-established that a person may die from poisoning and yet no poison be found by careful and accurate chemical analyses of the organs. This fact has, not infrequently, been overlooked in some cases where acquittal has resulted because the jury believed that, where no poison was found, none could have been taken and, in consequence, death could not have resulted from poisoning. In this connection Taylor[1] remarks: "Hence the statement that no person can die from poison, except the poison be found in the body, is a mockery, a delusion, and a snare, admirably adapted to cover a multitude of secret deaths from poison, which, but for this dogma, might be revealed by pathology and physiology. It is all the more dangerous, because the history of crime shows us that the arts of the murderer, especially of the scientific or professional murderer, are daily becoming more refined." It should, however, be remembered that, if the symptoms and the postmortem findings are not somewhat suggestive of poisoning, or at least compatible with it, the medical jurist is not justified in giving an opinion that death is due to poisoning in the absence of positive findings in the tissues. "Conjoined with strong moral circumstances, chemical evidence will often lead to conviction when the appearances in the body are entirely wanting, and the evidence from symptoms is imperfect"; yet, in such cases, this chemical evidence should be positive rather than negative.

While it is more or less commonly believed that the stomach and its contents is the only organ necessary to be examined in a case of poisoning, it should be stated that the liver, kidneys, and intestines should be submitted to the analyst in almost all cases, and in some special cases, the brain, spinal cord, heart and lungs. As previously stated, the poison found in the stomach has not been absorbed and is not, therefore, the toxic material that has caused death; while, on the other hand, that found in the liver, kidneys and other organs is the part that has been absorbed, circulated in the blood and been deposited in the tissues, in other words, is the part of the poison ingested that has caused the death in question. While, as stated above, no poison may be found in the body, yet it must be remembered that, if poison has been administered, it is more apt to have disappeared from the stomach by vomiting or absorption than it is to have been completely eliminated from the other organs. For this reason, one should always insist upon having the other organs mentioned for examination, if any real value is to attach to the report. Without some organ, other than the stomach or intestines, upon which he may conduct his analyses, the toxicologist is not warranted in stating from his positive finding of poison in the stomach alone that the person actually died from poisoning. All that he is justified in saying is that poison has been taken, but as to whether or not it has been absorbed and has acted as a poison in the body his examination will prove nothing.

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[1] *On Poisons*, 1875, p. 149.

In addition to the viscera, which are submitted to the toxicologist for examination, vomited matter, urine, suspected food or other material should, also, be subjected to close scrutiny, as these may reveal evidence which may prove very valuable later in the investigation. Careful search should be made of the premises in which the person died, in order to locate any possible poisons. The presence of such household compounds as "Rough on Rats" for instance may furnish the clue as to the source of an arsenical poisoning. Frequently the poisoner may carry the poison about in his clothes. Thus Mrs. Maybrick was accustomed to carry arsenic in her handkerchief; while Hoch of Chicago used the barrel of a fountain pen for this purpose.

It is clear that the one, to whom the analyses of the viscera in a case of suspected poisoning are entrusted, should be a chemist of experience, as well as a person with a good knowledge of anatomy, physiology, pathology, materia medica, and toxicology. While it may not be necessary that he be a graduate in medicine, yet, if he is, his general knowledge will be of great avail in unraveling some of the intricate threads of the skein of evidence. His integrity should be of the highest and, indeed, above the remotest suspicion, owing to the fact that his evidence may be the basis for an acquittal of an innocent person or the conviction of a guilty party. "Purely chemical evidence", says Witthaus, "is of fact rather than of opinion, and the chemical witness is 'expert' only in that he requires exceptional skill and training that he may ascertain the facts." It has been suggested that two chemists should conduct the analyses together and should conjointly give testimony regarding their results. While such a provision is probably, a wise one, yet it must be remembered that this may not only increase the time consumed in the analysis but, also, will perhaps more than double the expense. Further, it is not the number of experts that testify in a case that determines the value of the evidence, but, rather, the facts as brought out by such as are of unquestioned ability and integrity.

In those cases in which some indication of the poison to be sought may be given by the symptoms, postmortem appearances, or the circumstances surrounding the case, the analyst may direct his attention especially to this or closely related poisons. However, it is to be remembered that poisons do not always produce the same effects under all circumstances, nor will all individuals react in the same way toward the same poison, so that symptoms, as well as autopsy findings, can be regarded at most as suggestive. If several poisons are given together, the symptoms of each may be masked, so that a very confused train of symptoms may manifest themselves. For these reasons, it is wise, whenever practicable to so arrange the analysis that all types of poison will be covered and, in this way, to detect what poisons are present, if, indeed, they be detectable, and, also, to obtain evidence of the absence of certain other poisons.

The analysis should be conducted in a room in which other work is not going on and in one, which may be locked when the analyst is not present. No one, other than the analyst or his associates, should be present in the room during the examination, and, under no circumstances, should poisons, other than the reagents used in the tests, be kept in the examining room. It is important that all chemicals used in the tests should be known by the analyst to be pure and to contain nothing which might introduce errors into the tests as conducted. Blank tests should be run with the reagents and utensils used in the actual analyses, so that it may be clearly established that no poison is being introduced in the course of the examination. Great care must always be exercised to see that every article used in the tests is throughly clean and carefully washed free from all materials that may find their way into them.

Before starting the actual chemical examination of the various viscera submitted, the analyst should carefully inspect and weigh each organ, so that he may have definite data for his calculations as to amounts present in case of positive findings of poison. Fluid material should be measured also. If the contents of the stomach be at hand, this should be very carefully examined with the naked eye and, also, with a hand lens, for the presence of undissolved particles of poison, as this may give a clue as to later examinations. The presence of seeds, leaves, and other parts of poisonous plants should be noted, and the reaction of the contents should be determined. In case of poisoning with the cyanides, opium, carbolic acid, etc., the odor of the gastric contents may give valuable evidence. The nature of the food present in the stomach should be noted and its degree of digestion investigated, as this may prove of some value as evidence as to the possible time of death as related to the taking of food.

It is clear that the methods of analysis to be adopted by the toxicologist will depend largely on whether or not a single poison is to be sought or whether the examination is to include all groups of poisons. The object, in any case, is to separate the poison from the constituents of the organs in a sufficient state of purity to permit of its identification by physical, chemical, or biological tests. The substance to be examined should first be very finely comminuted, preferably in a hashing machine, and divided into at least 3 portions: (1) one part to be examined for volatile and mineral poisons; (2) one part to be examined for non-volatile organic poisons; (3) and the third part to be held in reserve for use in case of accident or if other tests should arise in the course of the case. If there is a possibility that corrosive substances may be involved in the case, a further portion may be necessary to cover this field of investigation. Whatever division of the material may be made, the part taken for any specific analysis must be accurately weighed or measured and its relation to the total weight of the organ or volume of liquid determined, in order that the future calculations may reveal the amount of poison in the organ or fluid involved.

Separation of Volatile Poisons.—Where qualitative results alone are sought for, it is not necessary that the material used be weighed out, but, as a rule, it is better practice to weigh out a definite portion of the finely hashed organ, so that the results obtained may be calculated on a quantitative basis, aliquot portions of the distillates being taken for the quantitative estimations. The weighed material is brought to the consistency of a thin gruel by the addition of distilled water and made slightly acid with tartaric acid if not already acid in reaction. If the material under investigation is in the form of a liquid, a definite fraction of the original amount is measured out and made acid if necessary. This material is then placed in an apparatus for distilling in steam and a Liebig condenser attached so that the distillate may be well cooled and condensed before passing into the receiving flask. (Fig. 34). Heat is carefully applied and the distillate collected in fractions of 50 cc. and the distillation continued until 5 such fractions are obtained. The regulation of the heat in the water bath and the current of steam should be so adjusted that the contents of the flask boil evenly and briskly. In order to prevent bumping in the distilling flask, a few short pieces of capillary glass tubing may be placed in the flask before applying heat. As a rule it is not necessary to take the temperature of the vapor distilling over, but, if a specific substance is to be looked for, a definite temperature of distillation may be advisable. Should the presence of phosphorus be suspected, the distillation should be conducted in a dark room and a screen placed between the flame of the lamp and the condenser, in order that any phosphoresence may be seen.

After the fractions from the acid solution have distilled over, the flame is turned off and the apparatus allowed to cool, when magnesia is added in sufficient amount to make the reaction of the mixture in the distilling flask feebly alkaline. This alkaline mixture is then distilled as was the original acid fluid, collecting at least 2 fractions of 50 cc. each.

The distillate from the acid mixture may contain alcohols, aldehydes, ethers, acetone, carbolic acid and other phenols such as the cresols, thymol and α and β-naphthol (the phenols with more than one OH group are practically non-volatile with steam); carbon disulphide; camphor and the essential oils; turpentine and other volatile hydrocarbons; chloral; chloroform; iodoform; nitroglycerin; nitrobenzol; benzoic acid; salicylic acid; hydrocyanic acid; hydrochloric and other volatile acids; and other less important volatile poisons. The distillate from the alkaline mixture may contain ammonia, aniline, coniine, nicotine, and other volatile bases. While some of the substances noted above may be found, also, in the later examinations for organic poisons, yet tests for any of the substances mentioned, if these be present in sufficient amount, may be obtained from the distillates by the methods outlined under the specific substance.

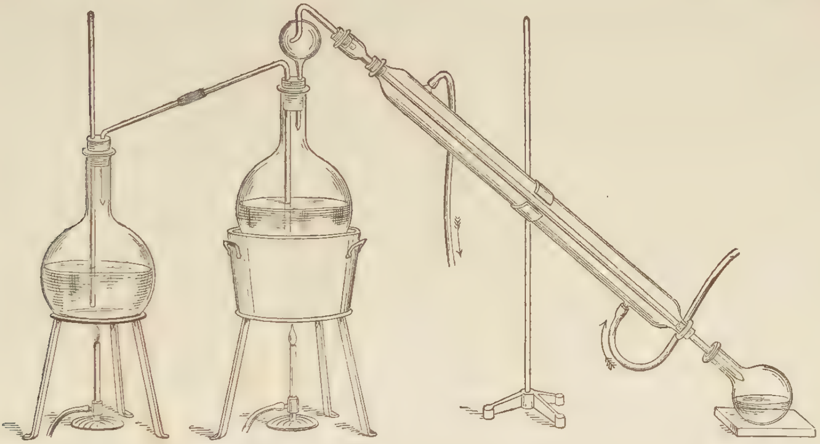

Fig. 34.—Apparatus for distilling in steam. (From Haines, in Peterson, Haines and Webster "Legal Medicine and Toxicology.")

After the completion of the distillation from the alkaline solution, the apparatus is allowed to cool and the contents of the distilling flask used directly for the determination of the presence or absence of mineral poisons. If one prefers, however, the material in the flask may be washed out into a porcelain dish for the later work, but, in most cases the flask is to be preferred.

Examination for Mineral Poisons.—The methods employed for the destruction of the organic matter, which is the first step necessary in this examination, are many, but we shall limit ourselves to the two which are more frequently employed than are the others.

Method of Fresenius and von Babo.[1]—This is the most frequently used and, probably, the best general method for destruction of the organic matter. The principle of the test is the addition to the material under examination of hydrochloric acid and potassium chlorate, which on heating liberate chlorine and oxides of chlorine, which compounds have a strong oxidizing action on organic matter.

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[1] Annalen d. Chem. u. Pharm., 1844, **49**, 308.

The material from which the volatile matter has been distilled in the previous process, or, if no examination for volatile poisons is to be made, a weighed portion of the finely hashed and thoroughly mixed substance is placed in a large flask and water added in sufficient amount to render the material gruel-like in consistency. Now add about ⅓ of its volume of chemically pure, arsenic-free concentrated hydrochloric acid and heat gently on the water bath. From time to time a small amount of potassium chlorate is added to the mixture in the flask and the flask shaken, the volume of the fluid in the flask being maintained by the addition of distilled water from time to time. The addition of the chlorate is continued until the mixture has a thin consistence, a uniform straw-yellow color, and no particles of organic matter are observed in the solution, except the white granular fatty material in suspension, which is not completely removed in this process. The heating should be continued until the liquid does not darken, if no chlorate be added, and the heating continued for at least ½ hour after the last addition of chlorate. It may, at times, be observed that the addition of chlorate produces no visible effect, in which case more hydrochloric acid must be added. It is important, however, that the amounts of both acid and chlorate added be kept at the minimum amount necessary to accomplish the destruction of the organic matter. This mixture is now filtered hot and the insoluble material on the filter is thoroughly washed with hot water. In the residue on the filter may be found any silver that may be present, in the form of the chloride, and more or less of the lead, barium and strontium, as sulphates, the amounts of these three latter metals depending upon the quantity of sulphates as such or produced by oxidation of the sulphur of the original material. As Haines remarks: "Barium and strontium are likely to be largely precipitated, but lead, unless in considerable amount, may pass entirely into solution, its sulphate being somewhat soluble in excess of warm hydrochloric acid, especially in the presence of chloride of sodium and potassium." To insure the complete precipitation of barium at this point, Autenrieth[1] advises the addition of a few drops of dilute sulphuric acid before filtration. It is important, therefore, that the material on the filter be examined for these possible metals, as otherwise they might escape detection.

The filtrate, which will contain all the metals present except those above-mentioned, is now heated and the excess of chlorine removed by passing a rapid stream of carbon dioxide through it. Now add sufficient sodium sulphite to cause the liquid to smell rather strong of sulphur dioxide, in order to convert any arsenic present from the arsenic form to the arsenous form, and heat gently until the odor of the dioxide has disappeared. If an excess of hydrochloric acid was used in the destruction of the organic matter, this filtrate will be, in all probability, too strongly acid to permit of the later precipitation of antimony and tin by the hydrogen sulphide. It is wise, therefore, partially to neutralize the excess acid with sodium carbonate and test a drop of this acid solution, on a porcelain tile, with a drop of a 1:12,500 solution of methyl violet; a blue-green color shows a satisfactory concentration, while a yellow or yellow-green color indicates too great an excess of hydrogen ions. A concentration of acid corresponding to a 0.25 molar solution is the most satisfactory for the precipitation of the sulphides of all the heavy metals, and such a solution gives the characteristic blue-green tint with the methyl violet indicator.

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[1] "Der Nachweis der Gifte auf chemischen Wege" in *Handbuch der Biochemischen Arbeitsmethoden* by Abderhalden, 1911, **5**, 762; *Detection of Poisons*, authorized translation by Warren, 6th ed. 1928, p. 242.

The flask, containing the filtrate treated as above, is placed on a water-bath and the temperature raised and maintained at about 70° C. A washed stream of arsenic-free hydrogen sulphide[1] is passed somewhat slowly through the solution for at least 1 hour, after which the heat is turned off from the water-bath and the solution allowed to cool gradually, the passage of the hydrogen sulphide being continued until the solution is cold. Now stopper the flask and set it aside over night. If the solution, on examination the next day, smells strong of the hydrogen sulphide and blackens a piece of filter paper moistened with a solution of lead acetate and held over the mouth of the flask, the precipitation of the sulphides may be regarded as complete, although it may be advisable, in case there is not an abundant precipitate, to pass the hydrogen sulphide again for at least ½ hour at 70°C. and then set the well-stoppered flask aside over night.

As soon as the sulphides have been completely precipitated in the manner outlined above, the contents of the flask are filtered and the precipitate well washed with water containing hydrogen sulphide. This precipitate contains, in case the acidity of the solution has been properly adjusted, the sulphides of arsenic, antimony, tin, mercury, lead, copper, bismuth, and cadmium, while in the filtrate are all the other metals, with exception of silver, traces of lead, part or all of the barium and strontium, which were previously retained on the filter when the original acid solution was filtered.[2] The separation and identification of these metals may be made according to the principles of qualitative analysis and will be taken up under the various poisons.

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[1] This arsenic-free hydrogen sulphide may be obtained by the use of arsenic-free ferrous sulphide and arsenic-free hydrochloric acid, both of which may be obtained on the market or this gas may be prepared in any one of the following methods: (1) prepare the gas in the usual way from ordinary ferrous sulphide and hydrochloric acid and pass it through a drying tube containing granulated calcium chloride and then through a tube of about 8 mm. in diameter and 40 cm. long loosely filled with solid iodine mixed with glass wool and, finally, through a wash-bottle containing a solution of potassium sulphide or potassium iodide; (2) saturate dilute sodium hydroxide solution with hydrogen sulphide prepared from the usual reagents. Place this sodium hydro-sulphide solution in a separatory funnel and allow this to drop into dilute sulphuric acid (1:4), when practically arsenic-free hydrogen sulphide will be evolved.

[2] It should be remembered that cadaveric material, even in the absence of any of the poisons above mentioned, when submitted to the Fresenius and von Babo method of destruction of organic material, frequently yields liquids which give yellow-red, or brownish-red precipitates with hydrogen sulphide, which precipitates consist of organic sulphur

Method of Gautier.[1]—The method, which we shall describe, is a modification of Gautier's original process and was devised, as was the earlier method, especially for the isolation of arsenic, but may be employed for the general detection of the other metals, with the exception of mercury which is partly, at least, lost by volatilization in this method.

Weigh out accurately 100 grams of the finely hashed material and place in a fairly large casserole. Upon this organic material pour from 30 to 60 grams of pure nitric acid, the amount depending upon the character of the material under investigation. To this add about 1 gram of concentrated sulphuric acid and heat on the water-bath until liquefaction occurs and the mass becomes thick. Remove the dish from the heat and add not more than 8 or 10 grams of pure concentrated sulphuric acid, stirring thoroughly. Now heat over the direct flame (but see that the heat is not sufficient to produce carbonization), remove from the heat and pour nitric acid over the material, a little at a time, until, upon heating the mixture to a point where thick vapors of sulphuric acid are given off, there is left in the casserole a brown liquid, which is practically uncarbonizable at the temperature at which sulphuric acid commences to boil. (It is probably needless to state that this process should be conducted in a hood with a good draught). When a point is finally reached where the nitric acid produces practically no further oxidizing effect, drive off the acid by heat, allow the material to cool, add a little sulphuric acid, and pour the brownish residue into 600 to 700 cc. of distilled water, stirring the water as the oxidized material is added. Thoroughly wash the casserole with distilled water and add this to the previous liquid. A finely divided brownish material falls to the bottom of the beaker, and the supernatant fluid is dark in color. Filter the liquid. On the filter will be found silver, lead, bismuth, tin, barium and strontium, while the filtrate will contain all the other metals (with the exception of mercury which is volatilized) and, possibly, traces of those largely retained on the filter. Neither this process nor that of Fresenius and and von Babo readily detect the presence of certain of the organic compounds of arsenic, for which special methods, to be discussed later, must be employed.

Detection of Organic Poisons.—Although some of the organic poisons are volatile and may have been separated by the process previously outlined for volatile poisons, yet some of these will also appear in the residues obtained by the method to be discussed. Aside from these,

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compounds and sulphur. Hence, the mere presence of a precipitate should not be taken as evidence that a metallic poison is present.

[1] Compt. rendus, 1899, **129**, 936. See, also, Gautier, Ann. de chim. et de phys., 1876, 5th ser. **8**, 384; Chittenden and Donaldson, Amer. Chem. Jour., 1880, **2**, 235; Gautier and Clausmann, Compt. rend., 1917, **165**, 11.

however, there are other important organic poisons, which may be divided into the following groups: (1) alkaloids and other basic substances; (2) glucosides and other neutral principles; (3) organic acids; and (4) oils, gums, resins, etc.

The first satisfactory method for extraction of alkaloids in toxicological cases was originated by Stas[1] for the detection of nicotine, but may be used for many of the other alkaloids. However, as this method does not yield the alkaloid in a very pure condition and, further, as many alkaloids are not readily soluble in ether, which Stas used as his immiscible solvent, Otto[2] advised the extraction of the final acid solution with ether, which removed coloring matter, glucosides and other non-alkaloidal substances and, thus, not only permitted the purification of the alkaloidal residues but, also, allowed of the detection of these other poisons, which were not found in the Stas process. This latter method is known as the Stas-Otto process and has found wide usefulness in toxicological work. There have been many later modifications of this combined process, which have been introduced to increase the possibilities of extraction by the use of different immiscible solvents.[3] However, inasmuch as the examination for alkaloids must, necessarily, be such as to include the largest possible number and, thus, permit of the isolation of any that may be the cause of the poisoning, the suggestion of Dragendorff[4], that both the alkaline and acid solutions be extracted with several immiscible solvents, is now generally adopted for routine work, although, if a single alkaloid is to be sought, the process may be considerably shortened by the direct use of the most appropriate solvent.

The principles governing the extraction of alkaloids by any of the modifications of the Stas process are the following: (1) Water or alcohol[5] acidulated with acetic, tartaric, hydrochloric, sulphuric, or other acid, extracts from the complex organic mixtures any alkaloids or other non-volatile organic poison present, together with some impurities, especially protids. Some of the constituents of the tissues under investigation are insoluble in the acid used and may be separated by filtration; (2) if the filtrate thus obtained is freed from alcohol (should this be used in the extraction) by evaporation and is then shaken with ether or other immiscible solvent, the glucosides and other non-alkaloidal organic substances are dissolved and pass into the immiscible solvent, which is separated from the acid aqueous solution, in which are to be found the alkaloids in the form of salts of the acid used in the extraction; (3) if this acid aqueous solution be made alkaline with ammonium hydroxide, potassium or sodium hydroxide (phenolic bases, such as morphine and apomorphine are not set free by these strong alkalies, but remain in aqueous solution as sodium compounds), sodium carbonate, or even by sodium bicarbonate in some cases, the alkaloidal salts present are decomposed and the free alkaloids, which are usually very slightly soluble in water, are liberated and may be thrown out of solution in the form of a precipitate or turbidity; (4) if this alkaline mixture is shaken with the immiscible solvent selected for the work, or with several in order, any alkaloids present will pass into the immiscible solvent in which they are soluble. The solvent is then drawn off and evaporated, when the free alkaloid, in a state of more or less purity, will be left behind and may be identified by tests to be outlined later.

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[1] Bull. Acad. roy. d. méd. de Belg., 1851, **11**, 304.

[2] Ann. d. Chem. u. Pharm., 1856, **100**, 44.

[3] See Rodgers and Girdwood, Pharm. Jour. and Trans., 1856, **16**, 1st ser., 497; Uslar and Erdmann, Ann. d. Chem. u. Pharm., 1861, **120**, 121 and Ztschr. f. anal. Chem., 1862, **1**, 267; Husemann, "Handb. der. Toxicol.", 1862, p. 202; Thomas, Chem. News, 1862, 341, 352; Marmé, Pharm. Ztg., 1883, **28**, 334.

[4] Ztschr. f. anal. Chem., 1866, **5**, 474; Ermittelung der Giften, 4te. Auf., 1895, p. 149.

[5] The ordinary commercial alcohol may contain basic substances as impurities, so that it is wise to purify it by adding tartaric acid (about 2 grams per liter) and allowing it to stand for 24 hours, after which it is distilled, repeating the operation a second time. Now add to the doubly-distilled alcohol a little pure sodium or potassium carbonate, to remove the traces of tartaric acid in the alcohol and again distill.

The method of choice in extracting practically all of the non-volatile organic compounds, which are involved in toxicologic work, is that of Dragendorff as modified by Haines, as this method not only permits of a sharp division of the poisons into groups but usually yields the alkaloids and other substances in a state of great purity.[1]

Haines' Modification of the Dragendorff Process.—Place a weighed amount (100 grams if this be available) of the finely hashed tissue in a 500 cc. flask and add about 3 times its volume of 50 per cent. purified alcohol acidulated with acetic or tartaric acid. Place the mixture on the water-bath and heat to a temperature not exceeding 50°C. for an hour or two. In order to avoid possible loss of material, one may connect a reflux condenser, but this is not usually necessary if the temperature of heating be carefully kept regulated. The mixture is then filtered, the insoluble residue being thoroughly washed with dilute alcohol, strongly pressed, again digested with acidulated spirit, and the liquid filtered and residue pressed as before, the operation being repeated several times to insure complete extraction. The united filtrates and washings are placed in a large evaporating dish and evaporated on the water-bath, preferably at a temperature not exceeding 60°C., to the consistence of a syrup, and, while it is still warm, three or four volumes of 90 per cent. alcohol are *very slowly* stirred in.[2] Allow the mixture to stand well covered in a warm place for at least an hour, stirring it occasionally. Now filter the liquid from the insoluble residue and digest and wash the latter repeatedly with slightly acidulated 90 per cent. alcohol. Again evaporate the filtrate and washings to a syrupy consistence, allow to cool, and when cold add slowly three to four volumes of absolute alcohol with constant stirring. Allow to stand for a few minutes and filter, again digesting and washing the insoluble residue with slightly acidulated absolute alcohol. Test a little of the filtrate in a test-tube with absolute alcohol, when the formation of a precipitate or a distinct turbidity indicates that the insoluble material has not all been removed. If this occurs, repeat the evaporation of the filtrate and the addition of absolute alcohol until all coagulable material has been eliminated. When this is accomplished, evaporate the final filtrate and washings to a syrup, allow to cool, and add two or three volumes of water acidulated with a few drops of sulphuric acid. Stir thoroughly, filter, and wash the alcohol-soluble but water-insoluble residue with water. Place this filtrate in a separatory funnel and proceed with the extraction with immiscible solvents.

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[1] "General Principles of Toxicology" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 57.

[2] If the alcohol be added slowly with constant sitrring, the precipitate of insoluble material is granular, but, if the alcohol be rapidly added, the precipitate is usually sticky and gummy and may enclose much of the soluble material thus causing more or less loss of possible alkaloids.

If a complete examination for non-volatile organic poisons is to be made, the acid liquid is first shaken out with petroleum ether in several successive portions until nothing further is removed as shown by leaving no residue on evaporation of some of the last extract. After the extraction with the petroleum ether, the acid liquid is extracted first with benzene (benzol) and then with chloroform, after which the acid fluid is again shaken with petroleum ether to remove traces of chloroform. Ammonia is now very carefully added to the acid liquid until the reaction becomes faintly alkaline, as shown by litmus paper. This alkaline liquid is then extracted successively with petroleum ether, benzene, chloroform, and amyl-alcohol, after which the fluid is evaporated to dryness with the addition of powdered glass, and the finely divided residue is extracted with chloroform. By evaporating immiscible solvents used in these extractions, residues are obtained, which may contain among others the substances mentioned below.

Petroleum ether extracts from the acid solution piperine, picric acid, salicylic acid, benzoic acid, camphor and ethereal oils, capsicin (capsicoside), and the esters of salicylic and benzoic acids with guaiacol, naphthol, and cresol.

Benzene extracts from the acid solution caffeine, geissospermine, traces of veratrine and hydrastine, piperine, canthardine, anemonin (anemonoside), santonin (santonoside), caryophylloside, cascarilloside, cubeboside, aloëtoside, elateroside, colocynthoside, populoside, digitalin (digitaloside), strophanthoside, picric, benzoic, and salicylic acids, traces of hydroquinon and resorcin, and salophen.

Chloroform extracts from the acid solution theobromine, colchicine, papaverine, narceine, hydrastine, cinchonine and cinchonidine, jervine, aspidospermine, and quebrachine, acetanilide, picrotoxin, colocynthoside, esculoside, and gelsemic acid.

Petroleum ether extracts from the alkaline solution coniine, nicotine, sparteine, lobeline, pyridine, aniline, kairine, thalline, phenocoll, antipyrine, aconitine, delphinine, and traces of strychnine, brucine, gelsemine, emetine, quinine, veratrine, and the alkaloids of quebracho and of geissospermum.

Benzene extracts from the alkaline solution strychnine, brucine, gelsemine, emetine, quinine, veratrine, and the alkaloids of quebracho and geissospermum, cocaine, atropine, hyoscyamine, hyoscine, physostigmine, eserine, pilocarpine, narcotine, codeine, thebaine, apomorphine, antipyrine, and thalline.

Chloroform extracts from the alkaline solution berberine, what is left of the cinchona alkaloids, of papaverine, and of narceine, and slight traces of morphine.

Amyl alcohol extracts from the alkaline solution morphine, solanoside, salicoside, and traces that may have been left of certain other bodies, such as narceine, cystine, saponoside (saponin).

Curarine is not removed by any of the above solvents, but is extracted from the residue left after evaporating the fluid with powdered glass by treatment with chloroform.

The residues obtained in the various extractions above mentioned are rarely of sufficient purity to permit of the substances being tested at once, but may require purification several times by dissolving them in acidulated water and shaking out with the appropriate immiscible solvent. In these shaking out processes, emulsions of the immiscible solvent with the aqueous liquids not infrequently are formed and may cause much trouble. To overcome these emulsions, one may add an additional amount of the solvent, may heat gently on a water-bath, may stir slowly with a glass rod, but occasionally none of these measures avail. As Haines points out,” the most satisfactory method is, as far as possible, to prevent the formation of the emulsion, and this can usually be accomplished by care in agitating the mixture. If, upon adding the immiscible solvent and shaking gently, it is seen that an emulsion is likely to follow, the agitation should be discontinued at once, the solvent allowed to separate, and after it has been drawn off a fresh portion poured in and again shaken gently.” It must be remembered, however, that in using this gentle shaking one must use repeated portions of the immiscible solvent to insure complete extraction.

Instead of shaking out with the immiscible solvents, somewhat quicker and often better results may follow the use of a perforator, in which the solvent is automatically and continuously carried through the aqueous liquid. Two forms of perforator are necessary, one to be used with liquids, such as ether, which are lighter than water, and another to be employed with liquids, like chloroform, which are heavier than water. (Figs. 35, 36.)

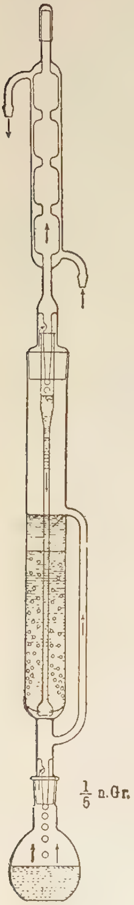

Fig. 35.—Kumagawa and Suto perforator for liquids lighter than water. (From Witthaus "Manual of Toxicology," Wm. Wood and Co., Publishers.)

In case only one or two specific poisons are to be searched for, the above process may be greatly shortened, the acid filtrate being purified by a preliminary shaking out with petroleum ether and then the best specific solvent for the poisons looked for being directly used either with the acid or alkaline solution as the case may be.

It is important to point out that, in any of these processes for extraction of the organic poisons, there may be considerable loss of the substance sought, especially in the processes of shaking out. "Every organic poison whether alkaloid or otherwise, and if alkaloid whether in the state of the free base or of a salt is invariably more or less soluble in every menstruum employed in purifying the material. It is commonly assumed that in shaking out an acid solution with ether, chloroform, or other immiscible solvent all of the alkaloid salt remains in the aqueous solution; but this is far from true, some of the alkaloid salt always being taken up by the immiscible liquid used. In this way a serious loss of the poison may occur, and if the amount originally present is small there may be even a complete failure to detect it, the losses being so considerable."

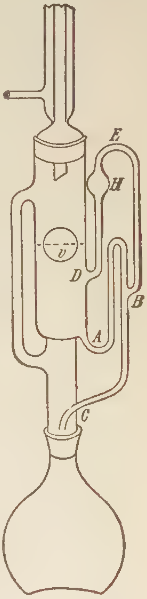

Fig. 36.—Osborne perforator for liquids heavier than water. (From Witthaus, "Manual of Toxicology," Wm. Wood and Co., Publishers.)

CLASSIFICATION OF POISONS

It is a difficult matter so to classify poisons that one can place in a certain group those that may not act, under certain conditions, in a manner which would properly classify it as a member of another group. If the classification is to be based upon effects produced, probably the most simple and useful one is the division into *corrosives*, *irritants*, and *neurotics*, but this separation is not entirely satisfactory.

As classifications based upon actions are, in practically all cases, faulty and, further, as such groupings do not always place similar chemical compounds in the same group and thus render the discussion of the chemical methods of detection and isolation somewhat complicated, we shall, for the purpose of this work at least, divide the poisons into (1) Inorganic poisons, including the corrosive acids and alkalies; (2) Gaseous poisons; (3) Alkaloidal poisons; and (4) Non-alkaloidal organic poisons.

FORENSIC QUESTIONS RELATIVE TO POISONING

In almost every case of poisoning which is investigated, certain questions of a medicolegal nature arise. While such questions are most frequently of importance in homicidal cases, yet they may arise in industrial, suicidal, or accidental types of poisoning, so that the expert must be prepared to meet them if occasion demands. The more important of these have been summarized by Haines and Webster[1] in a rather full manner, so that we shall follow this discussion in some detail.

1. Was the Death or Illness of the Subject Due to Poison? This is an extremely important question and one which arises in every case of suspected poisoning under investigation. It dominates all other questions and compels the expert to establish if possible, beyond a doubt, the fact that a poisoning has occurred. Outside of the circumstantial evidence, which is something with which the expert has to deal only indirectly, the demonstration of poisoning is definite when (1) the symptoms known to be caused by the poison have been noted during life; (2) the postmortem examination shows the presence of such lesions as the poison usually produces and the absence of other causes of death; and (3) the poisonous agent is shown to be present in the cadaver or in the vomitus or excretions of the person poisoned.

(*a*) The first indication of poisoning would probably be furnished by the nature of the symptoms shown by the victim; as a rule by their sudden appearance while he was in full health and, almost always, shortly after the ingestion of food or drink; by the violence and rapidity of these symptoms; and by their character, that is, by their primary localization and later generalization, followed frequently by a fatal termination. In chronic types of poisoning, such symptoms do not as a rule arise. In some cases of acute poisoning, the history of the symptoms is uncertain or obscure, while in other cases no symptoms at all may have been noted. In such cases collateral or circumstantial evidence may be very significant and may warrant a conviction, even though one of the cardinal points of the proof of poisoning is missing. If the subject does not die, the expert should remember that the symptoms observed are rarely sufficiently characteristic by themselves alone to justify a conclusion of poisoning as distinguished from disease.

(*b*) When death follows a suspected poisoning the autopsy furnishes a second point of evidence as to the cause of death. While inflammations of all degrees, interstitial hemorrhage, and fatty degeneration are the most commonly noted organic changes produced by poisons, yet certain poisons produce results which, while not absolutely characteristic, are however, extremely significant. Further, even when other causes of death than poisoning exist, these do not necessarily negative the possibility of poisoning. If poison be found in the body and signs of natural death also exist, it remains a question to be determined as to which of the two causes was operative. Postmortem findings are rarely conclusive since disease may produce the same appearances; but the lesions should be compatible with those produced by the suspected poison. In some cases the characteristic action of a poison may be absent, so that one should not be too quick to make his decision that a poison was not taken. Thus, in the Heidelmeyer case, which was one of known arsenic poisoning, the stomach and bowels showed not the slightest evidence of irritation, the mucous membrane being, in reality, paler than usual.

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[1] *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 69.

(*c*) The last determining element of poisoning, and, probably the most significant, is the finding in the body of the victim of a substance capable of causing the death. One should remember, in this connection, that the presence of a poison may be explained by some other cause than that of poisoning; and, further, it should be noted that, while the analyst may extract from the body the substance which exists in the organs, yet he is not always able to purify and identify it. In other words, a poison may be administered and none of it detected, owing to elimination from the body, or the substance may not be capable of chemical detection, although biologic tests may point to the presence of a toxic substance, whose nature is undetermined.

2. What Poison Produced the Illness or Death? This question assumes importance in every case of poisoning, especially of the criminal type. Although the toxicologist may, in his investigations, cover the entire field of poisons, yet his chief attempts are directed toward the isolation of a poison, which may cause the symptoms and changes observed. It is necessary that his findings be compatible with the symptoms and pathologic changes in order to establish the proof of poisoning. In some cases other evidence than that of finding the poison must assume great importance in order to insure a conviction, as the poison, even though it has been known that it was administered, may not be detected. Hence, the finding of a poison in the body is not absolutely essential to the establishment of the fact that a poisoning has occurred.

If the toxicologist isolates a poison, which may produce the symptoms noted and pathological changes found, then he is justified in stating that such a substance was responsible for the poisoning, but it must be remembered that the examination seldom reveals the exact form in which the poison was administered.

3. Was the Substance Employed Capable of Producing Death? This question raises the point upon which the definition of a poison is based. If the property of causing death or of injuring health was an essential and inherent characteristic of the substance itself, the question could be readily answered, but, it must be recalled that there are many factors which influence the action of poisons so that one is not in a position to state definitely that death would be produced by a given substance without knowing something as to the form in which the poison was administered and other factors previously discussed. Thus, while the soluble salts of barium are poisonous under certain conditions, the insoluble forms such as the sulphate may be taken almost with impunity without causing any sign of toxic action. Hence, one would not be justified in stating that barium was poisonous, without knowing in what form it was administered.

4. Was the Poison Taken in Sufficient Quantity to Produce Death? There are two factors that must be considered before one is justified in giving an opinion on the point involved: namely, (1) the lethal dose of the poison and (2) the amount actually taken in the case under investigation.

(*a*) The lethal dose of a poison is determined, within certain limits by observation of known cases of poisoning from definite amounts of the poison and by animal experimentation. It is true that, in most criminal cases at least, the amount of the poison which has produced death is unknown and that, only in very exceptional cases, is the analyst in a position to state how much of the poison was actually taken. If the toxicologist discovers, in his examinations, an amount of a poison, which is beyond the limits of the lethal dose of the poison as determined by either of the methods mentioned, he is certainly justified in stating that the quantity found is sufficient to account for the death. On the other hand, while his findings may be such as indicate a non-lethal dose, still the amount detected may be far in excess of the amount which would legitimately be present from ordinary medication or accidental impurities.

The expert is not infrequently asked as to whether he found sufficient poison in the stomach to produce death. It has been previously pointed out that the poison found in the stomach has, as a rule, very little to do with the actual poisoning, as the poison still in the stomach has not been absorbed and has, therefore, not produced toxic effects, except in case of corrosive poisoning. A very large amount of poison might be found in the stomach and yet the person may have died from some natural cause before absorption took place. In other words, a large amount of poison may be found in the stomach and little or none in the other organs examined. One would not be justified, therefore, in stating that he had found a lethal amount of the poison in such cases, as the substance is not a poison until it has been absorbed. This is the reason for insisting that other organs than the stomach alone be submitted for examination, as only by analysis of other organs can it be proven that the substance was actually absorbed. The toxicologist must find a lethal amount of the poison outside of the stomach and intestines, or else refrain from stating that he has found a lethal quantity. He is, however, justified in stating that the stomach contains a lethal amount of the poison, but he is not warranted in concluding that, from this fact alone, a lethal dose was actually absorbed.

(*b*) As to the actual amount of poison taken by the victim of poisoning it is difficult and, probably, impossible for the toxicologist to state. In the first place, the amount of a poison isolated represents only that obtained from a few organs, as the entire body is very rarely, if ever, examined. This amount may be a fatal dose or it may be very small. Secondly, the amount isolated represents only that which still remains in the body, the amount lost by vomiting, purging, and elimination through other channels not being determined. All that the analyst is justified in stating is that he actually isolated a certain amount and that the amount taken was, necessarily, larger than he obtained. If the amount obtained was a lethal quantity, he may, of course, so state;

while, if he has not obtained a lethal amount, he might give his opinion that a lethal amount had been taken, basing his conclusions upon known facts of general distribution of the poison throughout the body and upon the knowledge of elimination. It is not necessary that a lethal amount of the poison be found by the analyst, in order to establish the fact of death from the poison isolated, yet if such be found the case is greatly strengthened. If the quantity found be small, the analyst may be in a position to state that the frequency and amount of vomiting, the degree of purging, and the time elapsing before death took place were sufficient to account for the elimination of a large part of the poison ingested.

5. When and How was the Poison Taken? In criminal cases, especially, it is important to establish, if possible, the exact time of the commission of the crime, that is the time when the poison was administered. In most cases, this is a very difficult matter, as most poisons are administered secretly to the victim. The mode of onset, the rapidity of the appearance of symptoms, and the continuance or remission of these symptoms furnish evidence as to the approximate time of administration. While most poisons act rapidly, some more so than others, yet there are occasional cases reported in which the symptoms did not appear for several hours after taking the poison. However, such cases are the exception, so that the time of administration may generally be set down as within an hour of the appearance of the first symptoms.

Most poisons are taken by mouth. The symptoms, of course, appear much quicker when the posion is inhaled or given intravenously or hypodermically, so that, if the time of appearance of the first symptoms is known, one may have to take the route of administration into consideration in forming his conclusion as to the time when the poison was used. Some poisons, especially arsenic and morphine, are excreted into the stomach when administered parenterally, yet, as a rule, the finding of a poison in the stomach points to its administration by mouth. On the other hand, failure to find the poison in the stomach does not necessarily indicate that it was not given by mouth, as the absorption may have been complete or there may have been total loss by vomiting.

6. May a Poisoning Have Occurred and the Poison Either Be or Have Become Undetectable? There are a certain number of poisons which are not determinable by chemical means at present known or are converted in the body after death into substances which are normally present; other poisons are not capable of detection by physiologic tests, either because they show no characteristic symptoms or because the symptoms have been insufficiently studied; while there are but few which are shown conclusively by pathologic examination. Hence, it is clear that a poison may be administered and may escape detection by any or all of the methods available. One can not state in any specific case just how long after administration of a poison it will be deposited in the tissues, nor how long a poison once deposited will remain in the tissues, as poisons differ materially in the rapidity of elimination, both as regards the commencement and completion of the eliminatory processes. Poisons may be removed from the stomach and intestines by repeated vomiting, purging, and absorption, so that none will be found in these organs when examined. Further, if life continues long enough, all of the poison may be eliminated from the body. Moreover, organic bodies, especially the alkaloids and glucosides, may be more or less rapidly changed by the putrefactive processes to other substances, which do not possess sufficiently characteristic reactions to permit of their detection. Volatile poisons, such as hydrocyanic acid, may disappear quickly and thus escape detection. The possibility of detecting inorganic poisons, after some time, is greater than is the case with organic poisons, yet neither of these groups may be detected owing to their complete elimination from the body.

7. May the Poison Extracted from the Cadaver Have an Origin other Than in Poisoning? It should be stated that the finding of a toxic substance in the organs does not of itself prove a criminal poisoning, even though all of the symptoms and pathologic findings associated with the administration of this poison be present. In the first place, one must admit that certain of our medicinal preparations occasionally contain impurities, which may be found in the examination of the organs and may have caused both symptoms and pathological changes referable to it. Secondly, there are quite numerous cases of mistake in filling prescriptions by careless druggists. If the amount of poison found be small, the question will usually arise as to the possibility of its source being other than in a criminal poisoning. Aside from mistakes in filling prescriptions, certain drugs used in routine treatment may be found in a cadaver after death and may lead to possible confusion, if the information is not given that such drugs were actually used in the handling of the case. Further, one must bear in mind the possible introduction into the body of small amounts of poisonous impurities with the food. Those habituated to the use of certain drugs may show them in their organs after death from other causes, so that this possibility must be kept in mind. Moreover, it must be remembered that poisons may find their way into the body after death, as for instance in the imbibition of arsenic from the soil, the intentional placing of poison in the stomach in order to cast doubt upon the actual cause of death, and, above all, in the use of such embalming fluids as arsenic or formaldehyde. It is, of course, almost impossible to determine that such poison was artificially introduced into the body after death instead of being taken as an actual cause of death.

8. May the Poisoning be Simulated? It is to be said that the symptoms may be simulated but that the pathologic and chemical findings cannot. However, it is conceivable that a person, who is feigning poisoning, may take a small amount of some poison and may die soon thereafter, in which case the poison taken may be found in the stomach and tissues. However, in such cases the small amount of poison found, the lack of compatible pathological findings, even in presence of some of the symptoms of the poisoning, which the subject has feigned, should put one on his guard as to the conclusions to be drawn. Further, if in such hypothetical cases the death is sudden, there will be found, in all probability, some distinct pathological basis for the death. The most usual cases, in which simulation of poisoning occurs, are in hysterical or hypochondriacal patients, who fancy that they are being poisoned, and such patients may even introduce poison into their food in order to cast suspicion upon some thoroughly innocent person.

9. Was the Poisoning Suicidal, Accidental, or Homicidal? The answer to this question does not, as a rule, devolve upon the medicolegal expert, as he is concerned only indirectly with the circumstantial evidence in the case. However, he may be of some assistance in pointing out the method of action of the poison in question, in giving evidence as to the rapidity of action, and showing that the physical properties of the poison were such that it would not have been taken by a person in full possession of his senses. Finding of the poison in household remedies, which the victim was accustomed to take, would be significient of homicide as would the finding of the poison in the clothing or other articles possessed by the one suspected of causing the poison. Thus, Mrs. Maybrick carried arsenic in a handkerchief and in the pocket of her dressing gown, and Hoch used the barrel of his fountain pen in which to carry about the arsenic, which he used successfully with several victims. In cases of suicidal poisoning, the large amount of the poison taken may be significant, but does not necessarily prove that it was not given with criminal intent. Accidental poisonings are usually associated with the mistaking of one bottle of medicine for another, although it must be admitted that poison may be placed in a bottle of medicine, which was customarily taken by the victim.

CHAPTER XVII

CORROSIVES

While strictly speaking, our definition of a poison may exclude corrosives as a class, yet all such substances are absorbed to a certain extent and, especially, when they are administered in such a degree of dilution that their intense and characteristic local action is avoided. Under these conditions of dilution and absorption, they may act as direct poisons in the sense of our definition, disturbing the acid-base equilibrium and, both in man and in animals, producing such symptoms as weakness, somnolence, coma and convulsions. However, in discussing the action of the corrosive acids and alkalies, we refer especially to their effects when taken in their concentrated form, although these effects are largely local.

The corrosives act immediately and energetically upon the tissues with which they come in contact, inducing disorganizing and destructive effects by their chemical action. The symptoms produced are of such intensity and violence that no remote phenomena of strict poisoning appear. When brought in contact with the skin, their destructive action is analagous to that of a burn, as discussed in an earlier section. The local effect of the acids upon mucous membranes is noted as a dry, cloudy, grayish-white coagulation, while that of the alkalies is observed as a swelling and clearing up of the mucous membrane with more or less of a dark color due to imbibition of altered hematin by the submucous structures. If taken into the mouth and swallowed, we may observe the appearances of a burn about the mouth and all portions of the alimentary tract may show marked corrosion. This corrosive effect in the stomach and intestines may result in perforation, or, if the patient survives the primary effects, may so destroy the activity of the gastric glands that slow starvation may result, or death may result weeks or months later from constriction of the esophagus. Of course, sudden death may occur rather frequently from shock or suffocation due to the intense swelling and edema of the structures of the throat.

CORROSIVE ACIDS

As a general rule, the chemical examination of the tissues for the mineral or organic corrosive acids is necessary only when the postmortem findings indicate that a corrosive has been employed. Even then, one may not always be able to detect the free mineral acids, as these may have been combined or converted into their salts, which are normal constituents of the tissues, so that only quantitative determinations of such salts would give evidence of value. In some cases, however, the free mineral acid may be detectable, especially in the tissues corroded. The free mineral acids may be detected by extracting a portion of the material under investigation with water and filtering. On adding to some of the filtrate a few drops of a 1:1000 aqueous solution of methyl violet a blue-green color will be noted if the acid is not very strong, while, if it be somewhat concentrated, the color tint will be yellow. Instead of the above indicator, one may use a few drops of a 1:1000 aqueous solution of methyl orange, when a red color appears in the presence of free mineral acids.

SULPHURIC ACID

This acid is widely used in the arts and industry, so that it is very easily obtainable. Although its action is immediate and extremely painful, yet it has been used in some homicidal cases and in many more suicidal attempts, while its accidental employment has rather frequently caused death. It has been given as a medicine, has been mixed with food, has been poured into the ear, given by enema, and injected into the rectum and vagina. Not infrequently malicious persons resort to its use, by throwing it (the so-called "vitriol throwing") at others either to disfigure the face or ruin the clothing. In chemical laboratories, workers using the concentrated acid may be severely burned by the breaking of flasks or other utensils containing it.

It is clear that not all cases of poisoning find their way either into the medical or legal literature, but in 1911 Witthaus[1] collected 388 cases of poisoning with this acid, 53 of which were homicidal, 189 suicidal, 99 accidental, and 47 of unknown origin. Homicidal cases are extremely rare in this country, only one case being found in the literature by Witthaus[2]; suicidal attempts are relatively infrequent, reports from the Medical Examiner's office in New York City and the Coroner's office in Chicago showing only 2 deaths in each city in the years 1918–20 and 3 deaths in 1925 and 2 in 1926 in New York City; while accidental deaths are very few, although many persons are burned externally with the acid.[3]

Properties.—Pure sulphuric acid is a colorless, odorless liquid of oily consistency, has a specific gravity of about 1.83 at 25°C., and contains not less than 93 per cent. and not more than 95 per cent. of H_2SO_4. The commercial acid, known as "Oil of vitriol" is not so pure, is usually colored brown or, occasionally, almost black from the suspended carbonaceous matter, and contains small amounts of such metals as lead and arsenic. When the acid is added to water, heat is generated to such an extent that the mixture may boil if the proportion is about 3 of acid to 1 of water. The acid has marked power of abstracting water from substances with which it comes in contact, blackening or charring of the substance being observed. If the concentrated acid is heated with zinc, carbon, copper or other metals, sulphur dioxide is evolved; while if the acid be dilute, the gas given off is hydrogen. A stronger form of the acid, known as fuming or Nordhausen sulphuric acid, is in use in certain chemical processes, such as the manufacture of indigo, and has the formula $H_2S_2O_7$. Two forms of sulphuric acid are at times used in medicine, namely, the dilute acid (10 per cent.) and the aromatic acid (20 per cent. of free sulphuric acid and ethyl-sulphuric acid together).

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[1] *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 1911, **4**, 228.

[2] *Loc. cit.*, p. 229, whereon reference is made to the case of State *v.* Dinsmore, 61, Neb., 418. Beck (Medical Jurisprudence, 12th ed. 1863, **2**, 464) states that a woman was tried in New York state in 1817 for poisoning her illegitimate child with sulphuric acid, but we have not been able to locate the reference to it in the legal records.

[3] See McAllister, Jour. Amer. Med. Assoc., 1929, **92**, 1428, for a case of blindness.

Symptoms.—In contact with the skin, sulphuric acid produces pain and a burning sensation, with resultant corrosion and sloughing followed by a permanent scar. When the acid is taken accidentally, or even if given with criminal intent, the acid is seldom swallowed, as the person is immediately conscious of the severe pain and burning sensation in the mouth and throat. The parts, with which the acid has come in contact are corroded at once and show grayish-white patches, indicative of the coagulating and dehydrating action of the acid upon the tissues. The skin about the mouth may, also, show such grayish or brownish patches, which may become darker in color. Even in these cases in which the acid is not swallowed, death may occur rapidly as a result of edema of the glottis with associated asphyxia, although the acid is usually expelled so quickly that serious results do not obtain beyond the formation of permanent scars in the eroded areas.

If, however, the acid is swallowed, the effects are much more severe. At once there is intense local pain, extending from the lips, down the esophagus, into the stomach. The tongue may swell to a great extent and is, often, covered with the grayish coating of erosion. There is a profuse flow of saliva, but this is swallowed with difficulty and usually drools from the angles of the mouth. Thirst is extreme and, in a short time, severe vomiting ensues, the vomitus being slimy, very acid, brownish in color due to the presence of blood and much eroded tissue. The face has an anxious expression, the skin is clammy, the pulse is rapid and weak, respiration is gasping, and convulsive seizures may be observed. The urine is scant and must, in many cases, be withdrawn with a catheter, albumin and blood often being found, together with a marked increase of sulphates, but never free sulphuric acid. However, it must be stated that the urine may remain albumin-free, or, if it appears, it may disappear in a few days. Fraenkel and Reiche[1] report a case which even up to the time of death remained albumin-free, but which showed pathological changes in the kidney post-mortem. In the very acute cases, collapse may appear in a few hours or after several days and end in death. In some cases the corrosive action upon the stomach walls is so marked that, especially if the vomiting be severe, perforation and sudden collapse may appear. Should the individual survive the acute action of the acid (the mortality being about 70 per cent.), the corroded parts slowly undergo healing, but the damage done by the acid is evident in the constriction of the esophagus or of the pylorus and the more or less complete destruction of the glands of the stomach. For these reasons the individual usually suffers greatly from inability to swallow food and of digesting what food finds its way into the stomach and finally dies from inanition.

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[1] Virch. Arch., 1893, **131**, 130.

Fatal Dose.—It is a difficult matter to state definitely what the fatal dose of this acid is, as much depends upon the parts touched by the acid and on the amount of food present in the stomach. As Taylor remarks: "The dangerous effects of sulphuric acid appear to arise more from its degree of concentration than from the absolute quantity taken." It is conceivable that a very few drops of the concentrated acid might produce death, should the acid come at once into direct contact with the glottis, as edema would probably follow with a resulting asphyxia. The smallest fatal dose reported in a child was stated by Taylor[1] to be not over 40 drops of the concentrated acid ; while, in the adult, Christison[2] gives as the smallest recorded fatal dose 1 dram (3.8 grams), although an early case reported by Consbruch[3] of death from 20 drops may be possible even though the dose as given may be questionable. That it is not necessary that the concentrated acid be taken to cause death is shown by the reported cases of Heginbotham[4] of death in 2½ hours after swallowing of 22 cc. of the concentrated acid diluted with 66 cc. of water; of Wyss[5] of death in two months from two *swallows* of a mixture of one volume of sulphuric acid and four volumes of water; and of Mannkopf[6] of death in eight weeks after taking 15 to 20 cc. of the acid diluted with 5 volumes of water.

Fatal Period.—Death may result almost at once by the acid coming in contact with the glottis, causing spasmodic closure, as in a case in a child reported by Thomson.[7] Probably the shortest period recorded of death of an adult is that of the case of Rapp[8] in which death occurred in ¾ hour, while death has occurred in 4 cases in one hour, as mentioned by Witthaus. Probably the average period at which death takes place in acute poisoning from sulphuric acid is from 18 to 24 hours. In 160 cases collected by Witthaus, 16 died in less than 3 hours; 60 in 3 to 24 hours; 35 in 1 to 7 days; 18 in 1 to 4 weeks; 22 in 1 to 3 months; and 9 in more than 3 months.

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[1] *On Poisons*, 1875, p. 193.

[2] *A Treatise on Poisons*, 1st Am. ed., 1845, p. 131.

[3] J. d. pr. Arznk. u. Wundarznk., 1798, **7**, 2 st., 18. Cited by Witthaus, *Loc. cit.*, p. 234.

[4] Med. Times and Gaz., 1863, **1**, 183.

[5] Arch. d. Heilk., 1869, **10**, 184.

[6] Wien. med. Wchnschr., 1862, p. 564.

[7] Lancet, 1836–37, **2**, 359.

[8] Gaz. méd. de Paris, 1850, 3s. **5**, 926.

Treatment.—As the action of the acid begins at once and is most marked at first, treatment should be given as quickly as possible. Although some cases have recovered without any treatment whatsoever, yet it is true, on the other hand, that some cases have died which might have been saved by prompt treatment. The immediate need is to neutralize and dilute the acid, which is accomplished by giving milk in large quantity to which is added magnesium oxide. The carbonates or bicarbonates of sodium, potassium, calcium or magnesium may be given, if the magnesium oxide be not at hand, but it must be remembered that there is the possibility of increasing the distress and, even, of adding to the danger of perforation by the sudden liberation of carbon dioxide by the action of the acid in the stomach on the carbonates administered. Swallowing may be difficult, so that hypodermic administration of morphine or cocaine may control the pain and permit of the easy passage of the antidote. There is usually vomiting in these cases, so that emetics are contraindicated, especially owing to the danger of causing perforation. The passage of the stomach tube, in order to wash out the stomach, is always attended with more or less danger of perforation of the weakened wall of the stomach, but if used great care must be taken and the washing fluid should be small in amount and contain the antidote.

To relieve the intense thirst, ice may be held in the mouth. Pain is controlled by morphine, and nutritive enemata may be given. If signs of asphyxia appear, tracheotomy or intubation should be resorted to. The body temperature should be raised by external heat to the body and collapse controlled by appropriate stimulants. Should the person recover from the acute effects, the secondary action of the acid, in producing strictures of the esophagus or pylorus and in destroying the activity of the gastric glands, will, probably, require surgical measures of some type, although nutrition may be kept up, for a time at least, by nutritive pre-digested enemata.

The treatment of external sulphuric acid burns must be prompt in order to be effective. Water should be applied freely, the face or burned part should be immersed in water or held under a running tap, and the eyes opened under the water. A paste of sodium bicarbonate should be applied to the burned area to neutralize the residual acid. Later the area should be washed and treated with a bland oil or with *linimentum calcis*.

Postmortem Appearances.—The skin about the mouth may show brownish or brownish-black stains, which are usually in streaks due to the acid fluids drooling from the corners of the mouth. The lips and tongue are corroded and the latter may be swollen into an almost shapeless mass and be covered with a grayish coating. The mucous membrane of the mouth, throat and esophagus shows evidence of the corrosion in the grayish coating and, in places, deep corrosion, which may be so extensive that the entire lining of the esophagus has sloughed off. The stomach may appear, externally, partly brown and partly deep gray, while the mucous membrane is usually brownish-red, due to imbibition of acid hematin, or even black from charring. The gastric tissue is at first thickened but later becomes thin and soft. The pylorus may be thickened and parchment-like. In about ⅓ of the cases perforation occurs, so that destruction of the peritoneum and blackening of the organs from the acid stomach contents may be noted. Congestion, slight erosion and edema of the mucous membrane of the duodenum and upper parts of the small intestine may be observed. If sufficient acid passes the pylorus, the duodenum may show the same blackening and corrosion, with loss of the mucous membrane, that is seen in the stomach. "The parenchymatous organs and the musculature may show fatty degeneration and the lungs may show pneumonic processes."[1]

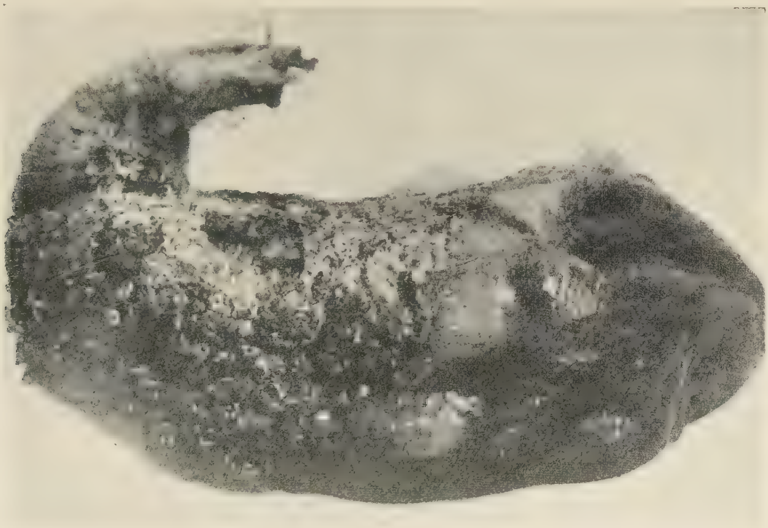

FIG. 37.—Stomach of a child showing the destructive effect of sulphuric acid (murder). (From Sydney Smith, "Forensic Medicine," J. and A. Churchill, Publishers, London.)

If the death has been due to the secondary changes instead of the acute form of poisoning, the usual appearances of death from chronic wasting disease are noted. The body is very emaciated, the eyes are sunken, and cicatrices may appear on the face as a result of the earlier burns. The throat may show some ulceration and scar formation; the esophagus is, usually, extensively ulcerated, much contracted, almost deprived of its mucous membrane, and very much thickened. The stomach is contracted as a rule, has lost most of its mucous membrane, and may appear reddish in color. The pylorus may be markedly constricted, as a result of which the stomach may be found dilated. In some cases the stomach may be found adherent to neighboring organs, as a result of old adhesions.

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[1] See *Lehrbuch der gerichtlichen Medizin* by von Hofmann, edited by Haberda, 11th ed., 1927, p. 808.

Detection.—While it is true that the free acid is rarely found in the stomach and its contents after death, yet this can not be taken as proof that corrosion and death from sulphuric acid has not occurred, although it does indicate the difficulty of showing by direct chemical analysis the presence of free sulphuric acid. Indeed, Buchner[1] has stated that "the chemical detection of a poisoning by nitric or sulphuric acid is, as a rule, impossible." However, that it has been and can be detected, even after some time has elapsed, is shown by reported cases, especially those of Lesser[2]. Probably the reason why the free acid is not more frequently found is because (1) it is neutralized by the antidote administered; (2) it is expelled by vomiting; and (3) it combines chemically with the constituents of the tissues with which it comes in contact. Garnier[3] believes that this is due to the reaction of sulphuric acid with the phosphates of the tissues, as a result of which free phosphoric acid is liberated. However, if an antidote were administered, the free phosphoric acid would be neutralized, so that we might not be any better off as to free acid.

A study of the circumstances of the death, of the pathologic findings, and an examination of any stains upon the clothing, will, usually, furnish very strong presumptive evidence. Further, a determination of the total amount of sulphates present in the tissues examined will, as a rule, indicate that such an amount could not be accounted for in any way other than by the administration of sulphuric acid.

The first step in the chemical examination for sulphuric acid is the determination of the presence of free mineral acid. Of course, one must remember that the stomach contents ordinarily possess a slight degree of acidity, so that the mere presence of an acid reaction in the stomach contents would have little value. However, other tissues are ordinarily alkaline, so that free acidity would be more presumptive in such cases, although, again, consideration must be taken of the fact that the body tissues tend to become acid after death until putrefaction changes them to alkaline again. In testing for free mineral acidity, extract a small portion of the material with water for some time, filter, and test portions of this filtrate with methyl violet, methyl orange, Congo red, or other indicator. If free mineral acid is present, then one has reason to test for free sulphuric acid as given below, but if no free mineral acid is found, then the tests must be directed to the detection and determination of the sulphates present.

To determine the presence of free sulphuric acid in the material under investigation, extract some of the tissue with water for some time and filter. This filtrate may then be tested for free mineral acids as mentioned above, and the following tests applied.

1. Evaporate a few cc. of the acid filtrate on the water-bath, adding a few crystals of granulated cane sugar when the solution becomes some-

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[1] *Lehrbuch der gerichtlichen Medizin*, 1867, p. 360.

[2] Vrtljschr. f. ger. Med., 1898, 3F., **16**, 76.

[3] Ann. d'hyg., 1884, 3S., **11**, 227; 1887, 3S., **17**, 148.

what concentrated. As evaporation proceeds, a black carbonaceous residue will be left in the presence of free sulphuric acid.

2. Evaporate a few cc. of the acid filtrate to a thin syrup and transfer the concentrated fluid to a test-tube, fitted with a cork through which passes a tube twice bent at right angles. Add a few strips of metallic copper to the fluid in the tube and heat, allowing the vapors given off to pass through the tube into a small amount of distilled water contained in a second tube. If free sulphuric acid be present, sulphur dioxide will be given off and may be tested for in the water solution in the second tube as follows: If a portion of the liquid be warmed with a little stannous chloride solution, a yellow precipitate of stannic sulphide appears. Instead of this test, one may add to the liquid in the tube a crystal of iodic acid and a little chloroform; shake the mixture thoroughly, when the aqueous layer becomes yellow, while the chloroform assumes a violet tint if free sulphur dioxide is present.

3. Evaporate a few cc. of the aqueous filtered extract of the tissue on a water-bath, add a small crystal of veratrine and evaporate to dryness, when the solution will be colored first yellow and the dry residue will show a crimson color throughout or, especially, at the edges, if free sulphuric acid be present.

Determination.—Extract a weighed amount of the finely divided tissue, or a measured amount of the fluid contents of the stomach, with distilled water, warming on the water-bath for a few hours. Filter, carefully wash the insoluble portion with water, concentrate the filtrate to about 100 cc. and place in a 100 cc. volumetric flask, making up to volume with distilled water. Measure out 50 cc. of this filtrate, place in an evaporating dish and evaporate to dryness, and treat the residue with a mixture of equal parts of alcohol and ether, stirring constantly. This process separates the sulphuric and phosphoric acids, from the insoluble sulphates and phosphates, the hydrochloric and butyric acids, which may have been present, especially in the stomach contents, having been volatilized. Filter the alcohol-ether solution into an evaporating dish, washing the residue on the filter with alcohol-ether. Evaporate this filtrate to a syrup on the water-bath, take up with a little distilled water and precipitate the sulphuric acid as barium sulphate in the usual manner. Filter and determine the weight of the dried barium sulphate by the usual methods of quantitative analysis, multiplying this result by 0.42 to obtain the amount of H_2SO_4 as such present in the 50 cc. of filtrate taken for analysis. If this latter figure be multiplied by 2, one obtains the amount of sulphuric acid in the weighed amount of tissue under investigation.

To determine the total sulphates present in the aqueous extract of the tissue, use the remaining 50 cc. in the volumetric flask, directly precipitating the sulphates with barium chloride solution, after acidifying the solution with hydrochloric acid. The amount of both free sulphuric acid and soluble sulphates is then determined as mentioned above, the calculations being figured so that the barium sulphate equivalent in H_2SO_4 is obtained. If the amount of free sulphuric acid, as obtained in the first process, be subtracted from the total sulphuric acid, as given by the latter method, one obtains the amount of sulphuric acid referable to the soluble sulphates.

It should, perhaps, be mentioned that if poisoning with lead or mercury be, also, in question, or there is reason to suppose that salts of either of these metals might be present, it is wise to precipitate the barium sulphate with barium nitrate solution in the presence of nitric acid instead of hydrochloric acid, in order to prevent the precipitation of lead and mercurous chlorides, which would, if present, lead to serious errors in the quantitative determinations.

NITRIC ACID

This acid is, like sulphuric acid, widely used in the arts and, in time of war, finds especial use in the manufacture of various types of explosives. From the reported cases one gathers that it is used more widely by suicides than by homicides, while the accidental cases are, probably, largely the result of inhalation of the fumes of the acid and the oxides of nitrogen, rather than the taking into the mouth of the free acid. In the early literature we find records of 55 cases collected by Tartra,[1] 26 of which were fatal. Since this time Witthaus[2] has found reported 85 cases of poisoning with nitric acid, 17 of which were homicidal, 43 suicidal, 14 accidental, and 11 of unknown origin.

Properties.—Pure nitric acid is a colorless, fuming liquid, very caustic and corrosive and having a characteristic, highly irritating odor. It has a specific gravity of about 1.40 at 25°C. and contains 68 per cent. of HNO_3. On long exposure to light and air, the acid becomes yellowish in color due to the formation of oxides of nitrogen. The commercial acid, known as *aqua fortis*, is somewhat weaker, containing about 40 per cent. HNO_3 and is usually colored yellow. Most metals dissolve in it with the evolution of brownish-red fumes of oxides of nitrogen, but gold and platinum are not attacked by it. It corrodes organic matter through its strong powers of oxidation, and does not carbonize as does sulphuric acid. It coagulates protein material and, if the acid be concentrated, a yellow color is produced, due to the formation of xanthoproteic acid. Occasionally, the spots on animal tissue may not be of the distinct characteristic yellow, but more of a yellowish-green tint.

Symptoms.—The effects produced by nitric acid, when taken into the mouth, are similar to those previously mentioned under sulphuric acid, except that the color of the lips and mouth, as well as the esophagus, is at first blanched and white, but soon changes to the characteristic yellow, while the coloration of the corroded areas of the stomach is less intense. There is marked pain, thirst, vomiting of bloody material containing shreds of tissue, and the same tendency to collapse previously discussed. With nitric acid, however, eructations of gas are much more frequently observed and the stomach may be distended with the gas.

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[1] "Traité de l'empoisonnement par l'acide nitrique." Thèse de Paris, 1802.

[2] *Medical Jurisprudence, Forensic Medicine and Toxicology*, 1911, **4**, 228.

Fatal Dose.—The determination of the exact quantity of any acid swallowed is a very difficult matter. Taylor[1] states that the smallest quantity which he found reported as destroying life is about two drams, which is confirmed by Kobert[2] (8 grams), and, probably, also by Warren[3], in his case in which a woman accidentally took 12 grams, of which some was spit out. As with sulphuric acid, a much smaller quantity might suffice to cause death from asphyxia, if it were to enter the larynx.

Fatal Period.—"This must depend on the quantity swallowed, the strength of the acid, and whether any medical treatment has or has not been adopted." While the average duration of life is about 24 hours, yet many of the cases are much more rapidly fatal and some are delayed for long periods, when death is due to the effects of the corrosion. The shortest case on record is that of death of an infant in a *few minutes*[4], while in an adult Taylor[5] refers to a case of Sobernheim of death in *one hour and three-quarters.* The most protracted case appears to be the one quoted by Tardieu[6] of death from starvation due to constriction of the esophagus at the end of two years. Of 54 fatal cases reported[7] death occurred in less than 3 hours in 5; 16 in 3 to 24 hours; 12 in 1 to 7 days; 7 in 1 to 4 weeks; and 14 in periods longer than a month.

Treatment.—The treatment of nitric acid corrosion is much the same as that of sulphuric acid. Probably little is accomplished by the administration of antidotes, as the action of the acid is marked and rapid. However, one should administer as rapidly as possible, alkalies such as whiting, magnesia in milk, soapsuds, and eggs. Of course, nothing is to be expected from such treatment beyond the neutralization of the acid that may remain; the corrosive action usually being manifested promptly. The general lines of treatment are as previously given.

Postmortem Appearances.—In case the acid is of a concentration less than 20 per cent., anatomical changes in the gastro-intestinal tract may be lacking. However, if over 33 per cent in strength, the early appearances are those of yellow coloration of the lips, mouth, throat, esophagus, and stomach, although this pure citron colon may be changed to a yellow-green. All the parts, with which the acid comes in contact, may show the signs of corrosion. Later may follow thickening and hardening, ulceration and sloughing, and perforations of the esophagus, stomach and intestines, although these latter changes are probably less frequent than is the case with sulphuric acid. The kidneys may be the seat either of coagulation necrosis or of acute parenchymatous nephritis.

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[1] *On Poisons*, 3rd Amer. Ed., 1875, 209.

[2] *Lehrbuch der Intoxikationen*, 1906, **2**, 36.

[3] Records Boston Soc. Med. Impr., 1853, **I**, 78.

[4] Taylor, *On Poisons*, 3rd Amer. Ed., 1875, 210.

[5] Ibid., p. 209.

[6] *Etude médicolégale et clinique sur l'empoisonnement*, *2eme ed.*, 1875, 238.

[7] *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 1911, **4**, 297.

Detection.—Ipsen[1] has shown that free nitric acid may find its way from the alimentary tract by diffusion after death, even in the absence of perforation, so that other organs than the gastro-intestinal tract may contain the free acid, although, of course, the stomach is more prone to yield chemical evidence. If antidotes have been given, then the tests must be directed toward the detection of the nitrates. Much of the acid is lost, of course, in combining with protein material to form xanthoproteic acid and nitro-derivatives.

To determine the presence of free nitric acid in the material under investigation, extract some of the ground tissue or of the contents of the stomach with water for some time and filter. Test the filtrate for free mineral acid as previously directed, and apply the following tests.

Instead of using the above simple method, which has the fallacy that other acid substances may be present, one may use the method of Baumert[2]. Neutralize the aqueous extract, as obtained above, with calcium carbonate, evaporate this material to a syrup and mix with 95 per cent. alcohol. Filter the alcoholic extract, evaporate to dryness, and dissolve the residue in water. Again filter and evaporate the filtrate to dryness. Dissolve this residue in alcohol and allow the solution to stand for several hours in a closed flask with about the same volume of ether. Filter this alcohol-ether solution, evaporate to dryness and dissolve the residue in a little water. The tests for detection are now applied to this aqueous solution of calcium nitrate, in case free nitric acid is present in the original material.

1. *Copper Test.*—Pour a few cc. of the filtrate into an evaporating dish and add a drop or two of sulphuric acid (free from nitric acid) if Baumert's method is followed, or if simple extraction with water has been employed no sulphuric acid is necessary, unless no free acid is present in this extract. Add a small piece of copper foil and warm gently. In the presence of nitric acid, effervescence and generation of reddish-brown irritating vapors will be noticed. If the acid is small in amount, the color of the fumes may be indistinct, in which case hold in the vapors a piece of filter paper moistened with potassium iodide and starch paste, when a blue color develops due to the liberation of iodine and the formation of iodide of starch.

2. *Diphenylamine-sulphuric Acid Test.*—Add a few drops of the reagent[3] to the aqueous extract and pour this mixture carefully upon pure concentrated sulphuric acid in such a way that a zone of contact is formed, when a blue color appears at the contact zone if nitric acid is present.

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[1] Vrtljschr. f. ger. Med., 1893, 3F., 6, 11.

[2] See *Detection of Poisons* by Autenrieth-Warren, 6th Amer. Ed., 1928, p. 293.

[3] Prepare this reagent as follows: Dissolve 1 gram of diphenylamine in a mixture of 5 grams of 10 per cent sulphuric acid and 100 cc. of water.

3. *Brucin Test.*—Place a few drops of the aqueous extract in an evaporating dish, add a drop or two of concentrated sulphuric acid and a crystal of brucin sulphate, when a blood-red color appears in the presence of nitric acid.

4. *Ferrous Sulphate Test.*—Place a few drops of the aqueous extract upon a white porcelain surface, add a drop of concentrated sulphuric acid and a crystal of ferrous sulphate. The crystal turns dark green and finally brown in the presence of nitric acid.

Determination.—Quantitative tests for nitric acid are rarely of value as there is considerable loss of acid in the combining with protein material. However, it may be necessary, in some cases, to determine the amount of nitrates present in order to arrive at a conclusion as to possible use of nitric acid. Under these circumstances the method of Dumreicher,[1] which depends upon the conversion of the nitric acid to ammonia, may be used. Thoroughly extract a weighed portion of the finely divided tissue or a measured amount of the stomach contents with water for a few hours. Filter, thoroughly wash the residue on the filter with water and follow Baumert's method (as discussed above) in obtaining calcium nitrate. Place the aqueous solution of the nitrate in a flask and add a freshly prepared solution of stannous chloride[2] and boil the mixture for an hour. Now pour this mixture into an evaporating dish, washing the flask thoroughly with water, and evaporate to the formation of a crystalline crust. Allow the dish to heat on the water-bath for ½ hour after this crust forms and then permit to cool. Now transfer this cooled mixture to a distilling flask, washing the dish thoroughly in order to remove all ammonium salts formed. Add sufficient solution of ammonia-free potassium hydroxide to render the mixture in the flask fairly strongly alkaline and distill the ammonia into a measured amount of normal sulphuric acid. Determine the amount of ammonia by titration of the residual acid with normal sodium hydroxide. The amount of ammonia found multiplied by 3.683 yields the amount of nitric acid, as HNO_3 in the weight of tissue taken for analysis.

HYDROCHLORIC ACID

Hydrochloric acid is a colorless, highly irritating gas, which is quite soluble in water. It is this aqueous solution of the gas that is usually meant when hydrochloric acid is spoken of. This acid is rarely used for homicidal purposes, although it finds more use by suicides than would be expected, while the accidental cases are fairly numerous. Death from hydrochloric acid seems to be somewhat prevalent in Great Britain, but in the United States very few cases occur, New York and Chicago each averaging about 1 death per year from suicide and 1 from accidental causes. Not including coroner's cases (of which there were 41 in the single year 1908 in Great Britain) Witthaus[1] has collected from the literature 126 cases of which 89 were fatal, 6 of these being homicidal, 57 suicidal, 40 accidental, and 23 of undetermined type.

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[1] Sitzungsber. d. k. Akad. d. Wissensch. z. Wien, 1880, **82**, 583.

[2] Dissolve 16 grams of pure tin in 60 grams of 40 per cent pure hydrochloric acid, using this amount for each gram of nitric acid suspected.

Properties.—The commercial hydrochloric acid, known as muriatic acid is a transparent, yellow liquid, containing about 32 per cent. of HCl and is contaminated with ferric salts and arsenic trichloride, along with other less important impurities. The so-called chemically pure acid is colorless, contains not less than 31 nor more than 33 per cent. HCl, and is usually contaminated with arsenic to the extent of approximately ¼ per cent. calculated as As_2O_3. Owing to this impurity, such acid cannot be used in the tests for arsenic without purification. The dilute hydrochloric acid of the U. S. Pharmacopoeia contains 10 per cent. HCl. The fumes of this acid are irrespirable and extremely irritating. The acid dissolves most metals, except gold and platinum. Normally, hydrochloric acid is found in the gastric juice to the extent of about 0.3 per cent.

Symptoms.—Inhalation of the fumes causes marked irritation in the throat and a sense of suffocation. If inhaled frequently, it may cause a chronic bronchitis and laryngitis. Taken in its liquid form, it acts as a corrosive but is not so severe in its action as either sulphuric or nitric acid. The mucous membrane of the mouth, throat and tongue are at first white and later become brown. Immediate pain along the track of the acid is noticed, swallowing becomes difficult, the voice is husky, respiration is accelerated and may be spasmodic, and cyanosis may appear as a result of the interference with respiration by the vapors of the acid. Severe epigastric pain, retching and vomiting may be observed, but in some cases the respiratory symptoms may almost mask those of corrosion. The pulse soon becomes weak and feeble, and collapse with death occurs, or convulsions may supervene. As with the other acids mentioned, if the patient survives the acute symptoms stricture of the esophagus or pylorus may result and the subject endure a long siege of inanition and ultimate death.

Fatal Dose.—Owing to the marked volatility of this acid, a little of it may prove rapidly fatal from spasm of the glottis. If the acid be rapidly swallowed, death has resulted from a dose of 1 dram (4 cc.)[2], while Kobert states that 10 grams of the raw commercial acid is sufficient, while Taylor says that "the smallest quantity which has been known to destroy life was about half an ounce of the strongest acid."

Fatal Period.—Death may occur rapidly from the suffocative effects of the acid. Christensen[3] has reported the death of a man, aged 24, in 1½ hours after taking about 200 cc. of this acid. However, the most of the cases do not prove so rapidly fatal, probably the average duration being about 24 hours. Of 71 cases found in the literature, of which the duration was noted, 2 died in less than 3 hours; 31 in 3 to 24 hours; 14 in 1 to 7 days; 10 in 1 to 4 weeks; 9 in 1 to 3 months; and 5 in more than three months.[1]

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[1] *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 1911, **4**, 228.

[2] Johnson, Brit. Med. Jour., 1871, **1**, 221.

[3] Ugeskrift f. Laeger, 1928, **90**, 86: Abs. in Jour. Amer. Med. Assoc., 1928, **90**, 1088.

Treatment.—The treatment, both local and general, is the same as has been discussed under sulphuric and nitric acids.

Postmortem Appearances.—The external burns and stains, which are so frequently found with the other mineral acids, are rarely noted with poisoning with hydrochloric acid, although Casper-Liman[2] report a case of a child 2 years old in which the skin of both cheeks and the chin were colored light yellow in many places. The signs of corrosion in the mouth, pharynx and esophagus are not so severe as with the other mineral acids, and the mucous surfaces have a white or brownish color instead of the black due to sulphuric acid or the characteristic yellow with nitric acid. The stomach may be normal or contracted, although very rarely it may be distended, and its mucous membrane is usually corrugated and hardened, yet this may rarely be thinned and susceptible to perforation, while the intestines have been perforated in two instances, as mentioned by Witthaus, and the corroded areas may be grayish in color as observed in a case by Hofmann.[3]

Detection.—Owing to the normal presence of hydrochloric acid in the stomach contents, the chemical detection of an abnormal amount of this acid is somewhat more difficult than is that of sulphuric and nitric acids, and requires a quantitative examination before anything significant can be assumed. Here, again, it must be remembered that the food may contain a large amount of chlorides, so that it is really only the free acid that is significant, and this must be present in relatively large amount before one is warranted in making a definite statement that the case is one of death from hydrochloric acid. If alkaline antidotes have been given to neutralize the acid, then the difficulties become greater than before.

1. *Silver Nitrate Test.*—Free hydrochloric acid or the soluble chlorides give with silver nitrate solution a white, curdy precipitate of silver chloride, which dissolves in ammonium hydroxide but is insoluble in nitric acid.

2. *Lead Chloride Test.*—In solutions which are not too dilute, a solution of lead acetate gives with free HCl or the soluble chlorides a white precipitate of lead chloride, which dissolves in hot water and crystallizes out from this solvent on cooling.

3. *Chlorine Test.*—Free hydrochloric acid, if warmed with finely powdered manganese dioxide or lead peroxide, yields chlorine, which may be recognized by its irritating odor and its yellow color, or by passing the gas into a solution of potassium iodide, when free iodine will be liberated. It must be remembered that the interaction of sulphuric acid with a

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[1] See Witthaus, *Loc. cit.*, p. 283.

[2] *Handb. d. ger Med.*, 8te. Aufl., 1889, **2**, 547.

[3] *Lehrbuch der ger. Med.*, by Hofmann-Haberda, 11te. Aufl., 1927, p. 810

chloride will yield HCl and will, therefore, yield chlorine when treated with the dioxides above mentioned.

Determination.—Weigh out a definite portion of the finely hashed tissue or take a measured portion of the stomach contents and extract with warm water for an hour or two. Filter this solution and divide into two equal portions. One of these is neutralized by adding an excess of sodium carbonate in order to fix any free acid present. Evaporate both of these solutions to dryness, when the unneutralized portion loses its free acid. Dissolve the residues in water and treat each with a solution of silver nitrate in the presence of free nitric acid, determining the amount of silver chloride formed in each case in the usual quantitative manner. In calculating the results, 100 parts of the dried silver chloride represent 25.43 parts of anhydrous HCl or about 80 parts of the concentrated 30 per cent. hydrochloric acid. The difference between the figures obtained with the two portions gives the amount of free HCl in the amount of tissue or fluid taken. If there is no difference, then the yield represents, of course, the combined HCl. In either case care must be taken in interpreting the results, as free hydrochloric acid is a normal constituent of the stomach contents and chlorides may be taken in large amount in the food and are found as normal constituents of all tissues.

OXALIC ACID

This organic acid and its salts are found rather widely distributed in nature, especially in such plants as rhubarb, nightshade, dock and sorrel, so that it may gain entrance into the human body from sources other than those associated with poisoning. It is a relatively frequent constituent of the urine of man, so that the finding of crystals of calcium oxalate in the urinary sediment can not be taken as evidence of poisoning with oxalic acid as is claimed in some of the older works on toxicology. The free acid, sometimes known as "acid of sugar", is used rather widely for its bleaching qualities and for its solvent powers for metallic oxides, so that it is readily obtained in the trade and from druggists.

Its use in homicidal poisoning is rather difficult, as its very sour taste, which is hard to disguise, enables its rapid detection by the victim. However, such cases do arise, Witthaus mentioning 12 of this type. Owing to its resemblance to Epsom salts, it is rather often mistaken for this latter substance, so that accidental cases of poisoning appear quite frequently. Poisoning with oxalic acid has been rather prevalent in England. Taylor says: "Oxalic acid is one of the most powerful of the common poisons; but its use as a poison is almost entirely confined to this country" (England). In the years 1871–80 in England and Wales, out of 1000 suicides by poison, 159 were traceable to oxalic acid. The reports of coroner's cases in the year 1908 alone, according to Witthaus, showed 81 cases, 70 of which were suicidal. While by no means all of the cases of poisoning from any substance find their way into the literature, Witthaus collected 242 reported cases previous to 1910, of which 134 were suicidal, 55 accidental, and 53 undetermined. In the United States, few cases are found. Thus, in the years 1870–1891 inclusive, there were 14 accidental deaths from oxalic acid poisoning in New York City; in 1918, 1 suicide; in 1919, 1 accidental death; in 1920, 3 accidental and 1 suicidal; and in 1926, 1 suicidal.

Properties.—Oxalic acid is a colorless crystalline substance, forming rhombic prisms or octahedral "envelope shaped" crystals. It is not deliquescent, but rather efflorescent. Its formula is $C_2H_2O_2 2H_2O$. It fuses about 98°C. and at a higher temperature it is decomposed into water, carbon monoxide and carbon dioxide. It dissolves in about 10 parts of cold water forming a very sour solution; is very soluble in alcohol, but very sparingly soluble in ether. Its salts, especially, the potassium binoxalate, are widely used in the household to remove rust and ink stains, to bleach straw, and to polish metals, so that it may easily be obtained for homicidal or suicidal purposes, and may, at times, be taken accidentally.

Symptoms.—Both the free acid and its soluble salts produce the same train of symptoms. According to the size of the dose and the degree of concentration of the solution taken, oxalic acid acts either as a corrosive or as a true poison, in the sense of producing effects resulting from absorption of the acid. If the solution be concentrated or if the acid or its salts be taken in the solid form, the symptoms observed are those of direct local action; while if the solution be dilute, the local symptoms may be entirely absent.

The local corrosive effects are usually immediate or appear, at least, in a few minutes. On swallowing a strong solution, there is a very sour taste, pain and burning in the mouth, throat and stomach, associated with a sense of constriction in the throat. There is difficulty in swallowing, and very soon vomiting of dark "coffee-ground" material of very acid reaction. The vomiting usually appears within 10 or 15 minutes, in some cases sooner, and in a very few somewhat later. Further, in some cases persistent vomiting and pain, later associated with persistent purging, may be the only marked symptoms noted, and the subject may die from exhaustion in some days. The pain is usually intense and of a distinct burning nature, although occasionally pain may be absent. The pulse is weak and irregular; respiration is shallow; and collapse with death may result in a very few minutes or be delayed for some hours or even days.

If the patient does not die rapidly from the immediate local effects, the true poisonous action resulting from absorption of the acid or its salts becomes manifest. The countenance is pale; the skin cold and clammy; pulse almost imperceptible; various muscles, such as those of the jaw and of both extremities, may be fixed in tetanic contractions; there may be general numbness and tingling and both abdominal and lumbar pain. The urine may be scanty or even suppressed, may show signs of severe renal irritation, and may contain large numbers of calcium oxalate crystals. Some cases may show violent tetanic convulsions, while others may react with stupor and become unconscious and die in coma.

When the amount of the acid taken is not sufficient to produce the violent corrosive actions mentioned above, the effects noted are almost entirely related to the nervous system, being either convulsive or narcotic according as the amount absorbed is relatively large or small. Whether or not convulsions or stupor and coma will be the salient features of the action, depend entirely on the amount absorbed, the symptoms in either case not appearing for some time, in contra-distinction to the almost immediate local corrosive effects.

Fatal Dose.—Although it seems from the reported cases in which the dose taken has been stated, that the most dangerous quantity varies from 15 to 30 grams, yet fatal poisoning has been observed with only 2 and 5 grams.[1] In one case death is said to have followed in nine hours after taking 4 grams (sixty grains) of oxalic acid.[2] It is probable that more than 15 grams would cause death in most instances, providing it is retained, but it must be remembered that recovery has followed from many times this dosage, owing largely to the prompt and vigorous vomiting which occurs.[3]

Fatal Period.—It should be mentioned that similar quantities do not destroy life in the same time in all cases. Thus an ounce of the acid has killed in thirty minutes in one case; in another in ten minutes; in other cases recovery has followed from such a dosage. Probably the most rapidly fatal case reported is that of Ogilvie[4] in which death occurred in 3 minutes. If death does not occur from the acute action on the gastro-intestinal tract, then life may last for some days or even recovery may follow. Of 86 fatal cases collected by Witthaus, 78 lasted less than 24 hours; of the 18 cases of longer duration, 3 died in 36 hours, 2 in 2 days, 2 in 3 days, 4 in 5 days, 1 in 6 days, 1 in 7 days, 1 in 8 days, 2 in 10 days, 1 in 14 days, and 1 undetermined.

Treatment.—The action of oxalic acid is rapid, so that whatever antidote is to be given must be administered promptly. Finely divided chalk or, if this be not available, wall-plaster may be chipped off and given. Sodium or potassium carbonates are of little avail, as the oxalates of these metals are readily soluble. While calcined magnesia or magnesium carbonate may be used, this is by no means as serviceable as are the calcium compounds. The antidote should be given in an abundance of water and should be followed by warm water to facilitate vomiting and washing out of the stomach. If it is necessary to induce vomiting, which is the case only if a relatively small amount is taken, probably apomorphine is to be preferred. Use of the stomach tube may be attended with danger. Symptoms must be treated as they arise.

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[1] See Hofmann-Haberda, *Lehrbuch der gerichtlichen Medizin,* 11te. Auf., 1927, 823.

[2] Barker, Assoc. Med. Jour., 1855, **2,** 1073.

[3] See Rost, Toxicology of oxalic acid and oxalates, Jour. Pharm., 1926, **29,** 257, for some interesting experimental work on animals.

[4] Lancet, 1845, **2,** 205.

Postmortem Appearances.—Oxalic acid does not corrode the lips and face, as do the mineral acids, so that stains are not present. However, the lips, tongue, mouth, and esophagus are of an opaque, usually white color, but this may exceptionally be of a yellowish-white tone, and show patches of a reddish tint. The mucous membrane is loose and eroded, and, in some places, may show thickening. The appearances of the mucous membrane of the stomach vary; in some cases it may be pale and smooth or detached in shreds; in other cases, it may be reddish and show distinct areas of corrosion; while in others it may be even black from extensive venous engorgement. Erosion is rarely so extensive as to produce perforation of the stomach, although this has been reported. The same appearances as the above may be seen, in some cases, in the duodenum and jejunum. As the elimination of oxalic acid occurs in the form of calcium oxalate through the kidney, it is to be observed that such crystals are to be found in the tubules and occasionally in the tissues, but probably never in the glomeruli. These oxalate crystals are rarely in the form of the perfect octahedra, but assume the more irregular shapes, such as long octahedra, needles, dumb-bells, whetstone and other shapes.[1] It is to be mentioned that none of these crystalline forms are stained in the usual pathologic staining processes, while calcium carbonate and phosphate are stained with hematoxylin.

Detection.—It must be borne in mind that the detection of traces of oxalates in the tissues is only of presumptive value in a case of poisoning, as these are found in certain foods and also as normal constituents of certain tissues, as a result largely of the metabolism of the nuclein substances. Further, in a case of poisoning the oxalic acid may exist (1) in the free state; (2) in the form of soluble oxalates; and (3) in the form of insoluble oxalates as a result of the administration of antidotes.

In obtaining the material for qualitative tests proceed as follows: Thoroughly hash the tissue to be examined. Treat this material with water at a gentle heat for a few minutes and test its reaction. If the reaction is acid, the material may contain the free oxalic acid. Filter the solution and evaporate to dryness on the water-bath. Extract the residue with alcohol, filter, evaporate to dryness and take up the residue with water, when the free acid will be found in this solution. Now filter from any insoluble residue. Extract this residue with alcohol acidulated with HCl, filter and evaporate the solution to dryness. Take up this residue with water, when the solution will contain the soluble oxalates. Now take the residues, insoluble in water and alcohol in the preparation of the two solutions above mentioned, and treat with an aqueous solution of potassium carbonate and boil for an hour or two. Filter the solution, evaporate the filtrate to dryness, and extract the residue with alcohol acidulated with HCl. Filter this acid-alcohol solution, evaporate to dryness, and take up residue with water, when a solution of the insoluble oxalates, which have been converted into soluble form, will be obtained. With these three solutions the qualitative tests for oxalates may be applied.

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[1] See Kobert, *Lehrbuch der Intoxikationen,* 1906, **2,** 76.

1. *Calcium Oxalate Test.*—Addition of an aqueous solution of a soluble calcium salt to a small portion of each of the three solutions, obtained as above, will yield a white precipitate of calcium oxalate, insoluble in ammonia or acetic acid, but soluble in hydrochloric acid, in case oxalic acid or its salts are present.

2. *Silver Nitrate Test.*—If a solution of silver nitrate be added to the suspected solution, a white precipitate of silver oxalate is produced, which is soluble in ammonia and in nitric acid. If this silver oxalate be dried and heated on platinum, it disperses with a slight explosion and a white smoke.

3. *Lead Acetate Test.*—If a solution of lead acetate be added to the suspected solution, a white precipitate of lead oxalate is formed, which is soluble in nitric acid, but insoluble in acetic acid.

4. *Potassium Permanganate Test.*—If a little of a solution of potassium permanganate and dilute sulphuric acid be added to the above solutions, the purple color of the mixture will slowly change to a colorless solution.

Determination.—Weigh out 100 grams of the finely hashed tissue and digest it with warm dilute hydrochloric acid until the tissue is almost completely disintegrated and the mixture is practically fluid. Filter and add to the filtrate sufficient ammonium hydroxide to produce a distinct alkaline reaction. Allow this mixture to stand over night, when it is filtered, the precipitate, if any, being quantitatively collected on the filter and thoroughly washed. This precipitate will contain any calcium oxalate existing in the tissues as such, together with other substances precipitable with ammonia. Save the filtrate for future treatment for the free acid in the original mixture and proceed as follows with the precipitate on the filter. Wash on the filter with acetic acid to dissolve other substances which have been precipitated, then remove the precipitate completely from the filter to a beaker by means of a stream of water from a wash-bottle. Add a little HCl and warm gently. Now add ammonia to the cooled solution and allow to stand over night, when the precipitate, which should be pure white, is filtered carefully and washed with water. This precipitate of calcium oxalate is then dried, blasted, and weighed in the usual manner as calcium oxide. To the filtrate obtained from the original precipitation with ammonia, add an excess of calcium acetate solution and allow the mixture to stand over night, when the resulting precipitate, if any, is filtered off and the amount of calcium oxide determined in the usual manner. In calculating the results, 56 parts of calcium oxide represent 90 parts of anhydrous oxalic acid or 126 parts of the usual crystallized $C_2H_2O_42H_2O$.

CORROSIVE ALKALIES

The strong alkalies, such as the hydroxides of sodium, potassium and ammonium, are markedly corrosive in action, this power being due to their solvent action on protein material, their saponifying action on the lipides, and their ability to extract water from the tissues. Their action as corrosives differ from that of the acids, in that the corroded areas are not dry and shriveled, but rather soft and gelatinous, the tissues being swollen, instead of contracted. The carbonates, and to a less extent the bicarbonates, are not only alkaline but have some corrosive effect, although less than have the hydroxides. The concentration of the alkaline solution causing the corrosive effects differs much in the various cases reported, most of those in Germany and Austria being due to the use of a 10–15 per cent. solution of sodium hydroxide, although some cases are apparently due to so-called "concentrated lye," whose strength may vary from 30 to 40 per cent or higher. For these reasons, it is a difficult matter to determine, in any specific case, just how much of the true alkali was taken, as solutions are almost always employed. There are a few homicidal cases reported, especially in children, while the suicidal cases are rather frequent, and the accidental ones quite numerous.

POTASSIUM HYDROXIDE

Properties.—The potassium hydroxide of the U.S.P. contains not less than 85 per cent. of KOH, and is a dry, white solid, fused in lumps or in sticks. When exposed to air, it rapidly absorbs carbon dioxide and moisture, and deliquesces. It has a soapy feeling, a soapy burning taste, and is strongly alkaline in reaction. It dissolves in about its own weight of water, and is soluble in both alcohol and glycerin, but insoluble in ether. On account of its rapid absorption of CO_2, the hydroxide may contain quite appreciable amounts of potassium carbonate. The official *Liquor Potassii Hydroxidi* contains about 5 per cent. of KOH and is a clear, colorless, odorless liquid, strongly alkaline and caustic. The so-called Vienna paste is a mixture of equal parts of potassium hydroxide and calcium oxide.

Symptoms.—Taken in strong solution, either the hydroxide or the carbonate will produce symptoms almost immediately. It causes a nauseous, soapy taste, associated with a burning pain in the mouth, throat, esophagus and stomach. Even should the solution be spit out at once, the parts touched will show signs of corrosion, the eroded areas being at first white, later becoming red or dark brown, and the parts will be greatly swollen. Soon thereafter, vomiting appears, the vomitus being alkaline in reaction and at first thick and slimy, later becoming dark in color due to the presence of blood and shreds of mucous membrane may be seen. Later abdominal pain, associated with purging of bloody material containing shreds of mucous membrane, follows. The pulse becomes feeble and rapid, the skin cold and clammy, the respiration rapid. The urine is scanty and strongly alkaline. As a rule the course is not so acute as with acid corrosions, death rarely occurring before 2 to 3 days, although some cases prove rapidly fatal, while Witthaus believes that death is rarely a primary result of the action of fixed alkalies. If the patient survives the immediate action of the alkali upon the stomach or the upper air passages, the patient may die days, weeks or months afterwards from the chronic effects of the strictures of the esophagus and pylorus.

Fatal Dose.—According to Mann[1] the smallest recorded fatal dose is 40 grains, although Holland[2] states "The ordinary fatal quantity is ½ ounce, but 30 grains have proved sufficient," but neither give any reference to the literature of these cases.

Fatal Period.—According to Taylor[3] the most rapidly fatal case reported is that of a boy, who died in 3 hours. Witthaus believes the reports of early death are not to be taken as indicating that death was due to the effects of the alkali, as in practically all of these there were some complicating factors. He states that "the most rapidly fatal uncomplicated case reported in the more modern literature is that of a boy of four years who died in collapse in fifteen hours." He further states: "Of seventy-one fatal cases in which the duration is stated, death occurred in less than twenty-four hours in seventeen; in from one to seven days in nine; in from one to four weeks in thirteen; in from one to four months in twelve; in from four months to one year in fourteen· and in periods longer than a year in six."

Treatment.—If the case be seen early the indications are, of course, to dilute and neutralize the alkali as rapidly as possible. The chemical antidotes should be the weak acids, such as acetic (vinegar), citric (lemon juice), or tartaric. If rapid administration of the acid has not been accomplished, the effects of neutralization will, of course, be very slight as the damage will have been done to the tissues. Bland substances, such as milk, olive oil, or melted butter may serve the purpose of both neutralization and soothing of the eroded surfaces. The intense pain may be controlled by opiates and the symptoms of collapse treated by appropriate stimulants. The chronic effects are to be handled as discussed under the acid corrosives.

Postmortem Appearances.—In the acute cases the epithelium of the mouth and esophagus are whitish or gray colored, swollen and soft. The mucous membrane of the stomach and intestines may be bright red or deep brown in color, the first due to hemorrhagic foci, while the latter color is probably due to the formation of alkali hematin. The tissues are swollen, more or less clear and soft. The walls may be contracted and the contents consist of a gelatinous, slimy, strongly alkaline, bloody fluid material, containing patches of eroded mucous membrane. The secondary changes observed, if death is delayed for some time, are stripping of the mucous membrane, ulceration and constriction of the esophagus and pylorus. In those cases which last for a few days, degenerative changes may be observed in the liver and kidneys and the lungs may show pneumonic processes.

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[1] *Forensic Medicine and Toxicology,* 1893, p. 419.

[2] "Inorganic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2,** 141.

[3] *On Poisons,* 3rd Amer. Ed., 1875, p. 250.

Detection.—It must be remembered that salts of potassium are found in all tissues to a certain extent, so that mere qualitative detection does not suffice to establish the nature of a case arising from corrosion with such compounds. In order to prove that the corrosive is really an alkaline hydroxide, this must be detected in its own form, as Witthaus remarks: "This, so far as we are aware, has never been accomplished in portions of the cadaver, nor is it probable that it will be, as during the survival of the victim it will be expelled by vomiting or converted into other forms of combination. Indeed, we know of but one instance in which the stomach contents have been found to be alkaline."

In detecting the presence of potassium hydroxide or carbonate, it may be possible to show such substances in the vomitus but, as mentioned above, it seems unlikely that we can expect much from the examination of the tissues. As the most characteristic reactions of the potassium ion are given, also, by the NH_4 ion, any ammonium salts present must be removed from the aqueous extracts by heating with calcium hydroxide before applying the tests. The usual qualitative tests used are (1) the hydrochlorplatinic acid test, which precipitates potassium from neutral or acid solutions in the form of a heavy yellow crystalline precipitate, insoluble in 80 per cent. alcohol; (2) addition to the neutral or alkaline solution of potassium salts of an aqueous solution of sodium hydrogen tartrate, when a white, granular, crystalline precipitate of potassium hydrogen tartrate forms; (3) addition to the neutral solution of potassium salts a few cc. of a solution of sodium cobaltinitrite, when a yellow crystalline precipitate of potassium cobaltinitrite is formed. When the sodium salts are present in large amount, this reaction is to be preferred to the hydrochlorplatinic acid test; (4) addition to the neutral, acid, or alkaline solutions of potassium salts of an aqueous solution of perchloric acid, when a white crystalline precipitate of potassium perchlorate is obtained.

Determination.—In any determination of the amount of potassium in the tissues, it must be remembered that various salts of this metal are present, having been taken in as food or in water, etc. Hence a quantitative determination is, at best, rather uncertain as to the amount of possible potassium taken as a corrosive agent. However, in some cases, such a determination is advisable and the usual method of precipitation as the potassium chlorplatinate and weighing as such is to be followed. If the amount of this chlorplatinate be multiplied by 0.1155 the result will be the amount of KOH as such in the amount of tissue taken for analysis.

SODIUM HYDROXIDE

Properties.—The sodium hydroxide of the U.S.P. contains not less than 90 per cent. of NaOH, and is a dry, white solid, fused in lumps or in sticks. When exposed to air, it deliquesces, absorbs CO_2, and becomes covered with a coating of the carbonate. It has a soapy feeling, a sharp burning taste, and is strongly alkaline in reaction. It is soluble in about its own weight of water at 25°C. and is very soluble in alcohol. The official *Liquor Sodii Hydroxidi* contains about 5 per cent of NaOH and is a clear, colorless, odorless liquid, strongly alkaline and caustic. Sodium carbonate, the ordinary "sal soda" or "washing soda" is a white, odorless, crystalline powder, which is efflorescent and not deliquescent as is the potassium carbonate. The carbonates are alkaline in reaction, have a sharp taste, are very soluble in water and exert a corrosive action, although this is less than that of the hydroxide. The sodium bicarbonate, ordinary baking soda, is less strongely alkaline and far less corrosive than the carbonate.

Symptoms.—Practically the same as those of potassium hydroxide although possibly not so marked. The sodium salts show practically no systemic or general reactions, while the potassium compounds may exert some depressing action on the heart and muscular system.

Fatal Dose, Fatal Period, Treatment, and **Postmortem Appearances** practically the same as for potassium hydroxide.

Detection.—Owing to the constant presence of sodium salts in the tissues and food, the mere qualitative detection of sodium proves little or nothing. In the presence of a strong alkaline reaction of the stomach contents, which will probably be found only in the case of the vomitus and rarely in the stomach contents after death, sodium may be detected by extracting with warm water, filtering and adding an excess of an aqueous solution of dipotassium dihydrogen pyro-antimonate and allowing to stand for some time, possibly even over night, when a white crystalline precipitate of the disodium dihydrogen pyro-antimonate will form. This precipitate is always crystalline and may not form at all in very dilute solutions. The solution to which the pryoantimonate is added must be either neutral or alkaline, and not acid. Hence, if free acid be present, this must be neutralized by the addition of potassium carbonate in excess before adding the pyroantimonate. It is occasionally necessary to remove all other cations than those of sodium and potassium before making this test, as they may greatly interfere by preventing the precipitation. A further test for the presence of sodium salts is the flame test, these salts imparting an intense yellow color to a colorless flame.

Determination.—It is probable that quantitative determinations of sodium are rarely called for in such cases, but should occasion arise, the usual methods of quantitative analysis must be employed.

AMMONIUM HYDROXIDE

Ammonium hydroxide is rather widely used in the household in the form of "hartshorn" and "ammonia" for cleaning purposes, so that it is easily available for use in poisonings of various types. Probably the larger number of cases of death from ammonium hydroxide are accidental, although many are suicidal. The widespread use of liquefied ammonia gas in the manufacture of artificial ice has lead to many deaths from suffocation as a result of bursting of the receivers. Of 83 cases in which the causation was given, Witthaus found 49 accidental cases, 27 suicidal ones, 5 homicidal, and 2 to produce abortion.

Properties.—The gas (NH_3) is a colorless, pungent, irritating gas, which is lighter than air and has a distinct alkaline reaction. This gas is very soluble in water, to which it imparts the strong alkaline reaction. The solution in water is known as ammonium hydroxide (NH_4OH), a 28 per cent. solution of which constitutes the *Aqua Ammoniae Fortior* of the Pharmacopoeia, while the *Aqua Ammoniae* is a 10 per cent. solution, and the Spiritus Ammoniae Aromaticus is of somewhat less strength. The strong solution of ammonia has the pungent, irritating odor of the gas and has a very caustic alkaline taste. The official carbonate is a white, hard, translucent powder, yielding about 31 per cent. of NH_3. The carbonate is in reality a mixture of true ammonium carbonate and ammonium carbamate, and yields to water and alcohol its volatile principles, being widely used in the form of "smelling salts."

Symptoms.—The nature and extent of the action of ammonium hydroxide will depend on the strength of the solution used and, also, upon the method of administration. If the vapor is inhaled, the action is largely limited to the mucous membranes of the respiratory tract. The action here is largely irritating rather than corrosive and the mucous membrane is swollen and softened, the respiratory symptoms being first manifested as a suffocative feeling due to spasm of the glottis, followed by pain and a sensation of weight in the chest and difficult breathing with an irritative cough resulting from irritation of the larynx and trachea.

If the liquid form be swallowed, the symptoms are much the same as those noted with the other corrosive alkalies, although probably somewhat less in degree. Almost immediately there is a sensation of burning pain in the mouth and throat, extending to the stomach if the fluid reaches this viscus. The epithelium is eroded, usually reddish in color and markedly swollen. There is vomiting and difficulty in swallowing, but these findings are less marked than the symptoms related to the upper areas, although if a large amount of the hydroxide reaches the stomach, the mucous membrane may be much eroded and swollen. The general effects may be rather marked. The urine is scanty and contains albumin and casts, at times blood cells. The action of the heart may be suddenly arrested and death may occur from syncope; or coma with convulsions may supervene. Probably the most frequent cause of death is sudden suffocation. If the patient survive the immediate effects, the later symptoms are related to the inanition and collapse resulting from stricture of the esophagus and pylorus.

Fatal Dose.—It is probable that a relatively small amount of the strong ammonia water would cause death if inhalation resulted in spasm of the glottis, so that in such cases it is almost impossible to state the fatal dose. By a combination of the effects on the upper air passages and the stomach, death has resulted from a teaspoonful of the stronger aqua ammoniae in one case reported by Stevenson[1], Tardieu[2] refers to the death of an adult from 15 grams of an ammonia of unstated strength, while Lesser[3] records the death of a child of two years of age from 1.5 grams (24 minims) of ammonia of 10.2 per cent. strength. It should be remembered, however, that recovery has occurred from much larger doses, as, for instance, 1 ounce in several cases.

Fatal Period.—Probably the most rapidly fatal case reported is the one of Stevenson referred to above, in which the man, after taking the teaspoonful dose, complained of some abdominal pain, turned on his side and died almost at once without any struggle for breath. "The prognosis when aqua ammoniae has been swallowed appears to be more favorable than when the fixed alkalies or mineral acids are similarly taken." According to Witthaus, death from secondary effects is rarely to be expected, as he was able to find only one case of death in three months[4] from the protracted effects, although he refers to a case mentioned by Tardieu[5] of death in 45 days from the *primary action* of 45 grams of aqua ammoniae.

Treatment.—The immediate treatment is the same as with the fixed alkalies. Suffocation may be combated by inhalation of oxygen or by artificial respiration, while symptoms are to be handled as they arise.

Postmortem Appearances.—These are much the same as with the fixed alkalies, although the upper passages usually show a marked change in the epithelium of the mouth and throat, this appearing as a red, inflamed, softened and swollen area. The mucous membrane of the stomach may be almost black, due to the marked bloody exudate. The upper air passages may show inflammation and edema, while the bronchi and lungs may also be edematous and congested. The kidneys may, at times, show a glomerulonephritis.

Detection.—Owing to the volatility of ammonium hydroxide, as well as the carbonate, these compounds may be absent from the stomach contents, unless the examination be made soon after death. If antidotes have been administered, then, of course, the free hydroxide will have been converted into the salt and the free alkali reaction lost. Fortunately, however, ammonium salts are volatile and yield ammonia, especially when heated with calcium hydroxide or other alkali. If some of the suspected material be placed in a distilling flask, some alkali added and heat applied, ammonia will distill over and may be detected by the following tests. (1) The vapors will color red litmus paper blue; (2) if a rod moistened with concentrated HCl be held in the vapors, dense fumes of ammonium chloride will be noted in the presence of ammonia; (3) hydrochlorplatinic acid yields a yellow precipitate with the distillate; (4) if some of the distillate be added to Nessler's solution, a brownish color or a red-brown precipitate may be observed; (5) if a solution of mercurous nitrate be added to a little of the distillate, a black precipitate will be noted.

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[1] Guy's Hosp. Rep., 1871, 3 S., **17**, 225.

[2] *Etude médicolégale et clinique sur l'empoisonnement,* 2eme. ed. 1875, 317.

[3] Vrtljschr. f. ger. Med., 1898, 3F., **16**, 89.

[4] Barclay, Med. Times and Gaz., 1853, **2**, 554.

[5] *Loc. cit.*, p. 317.

Determination.—Quantitative determinations are rarely of value, especially if the examinations are made some time after death, as the ammonia originally present may have escaped and, on the other hand, ammonia may have been formed in the processes of putrefaction, so that, in either case, the results will be erroneous. If the organs are obtained soon after death and if death has occurred fairly soon after taking the corrosive, then some value may attach to such examinations.

If free ammonia is present in the stomach contents or in the organs submitted, the finely hashed tissues are carefully weighed, treated with absolute alcohol, as advised by Vitali, and a little ether added. If this mixture be distilled at a temperature not exceeding 40°C., the free ammonia will distil over with the ether, and the distillate may be received in a known amount of normal or N/10 sulphuric acid. If the distillate be then titrated with a normal or N/10 solution of pure sodium hydroxide, the amount of ammonia passing over may be calculated.

If no free ammonia be present in the tissues or stomach contents, weigh out a definite amount of the material, place in a distilling flask, alkalinize with strong sodium hydrate and distil at boiling temperature, allowing the distillate to pass into a known amount of standard sulphuric acid. By back titration with standard alkali, the amount of ammonia liberated may be calculated.

Instead of using the above method, one may neutralize the distillate with hydrochloric acid and determine the ammonia as ammonium-chlorplatinate in the usual manner.

CHAPTER XVIII

NON-METALLIC POISONS

THE HALOGENS

Chlorine, iodine and fluorine are normal constituents of the organism, chlorine being found in all tissues, iodine being practically limited to the thyroid, and fluorine being present in the bones and teeth. Bromine does not appear to be found normally in the body, although under certain conditions it may replace the chlorine of the gastric juice and of some of the tissues. All four of the halogens, when in the free state, are locally irritating, a property possessed by both their hydrogen and oxy-acids. When in strong solution, the haloid salts act as strong irritants to the mucous membranes, while in dilute solution each has a more or less specific action. The organic halogen derivatives usually show a narcotic effect.

CHLORINE

Chlorine is widely used in the arts as a bleaching agent, in the household both as a bleaching agent and disinfectant, and in sanitary engineering as a disinfectant in the purification of water supplies. In the World War it found wide use, on the Ypres front especially, as an asphyxiating gas, which caused very great havoc. It has been advocated in the treatment of respiratory infections, but has not proven successful for this purpose.

While free chlorine has not been used for homicidal or suicidal purposes so far as we have found from the literature, yet at least seven cases[1] of accidental acute poisoning from inhalation of chlorine have occurred among operatives in factories. An interesting case of industrial poisoning from low concentration of chlorine gas, where the exposure continued for a period of years, has been reported by McCord.[2] Several other cases, some of them homicidal, have been reported from the administration of alkaline preparations, which yield free chlorine.

Properties.—Chlorine is a yellowish-green gas, which has a very penetrating, irritating odor. The gas is 2½ times heavier than air, is a very energetic chemical agent, is very soluble in water and may be compressed to a liquid. It is made in the laboratory by several methods, but the chief source in the household is the *Calx chlorinata* (chlorinated lime) of the Pharmacopoeia or the sodium hypochlorite of the trade.

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[1] See Witthaus, *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 1911, **4**, 335.

[2] Jour. Amer. Med. Assoc., 1926, **86**, 1687.

Other official preparations, which may be used to furnish chlorine for general use, are *Liquor Sodae Chlorinatae* (Labarraque's solution), *Liquor Sodae Chlorinatae Chirurgicalis* (Modified Dakin's solution), *Chloramina* (Chloramine-T) and *Dichloramina* (Dichloramine-T). An unofficial preparation is *Eau de Javelle* (Javelle water), which is to all purposes the same as Labarraque's solution, although the former is properly speaking a potassium compound. All of these products either liberate chlorine on exposure to air or on addition of a strong mineral acid.

Symptoms.—If inhaled in small quantity, chlorine causes a feeling of suffocation and an irritative cough. If inhaled undiluted, it produces almost at once immediate spasm of the pharyngeal and laryngeal muscles, pain in the chest, marked dyspnea, cough, occasional vomiting, cyanosis, and collapse. The pulse is weak and rapid and the respiration very dyspneic. The cough is intense and persistent, resulting in little expectoration, although occasionally some bloody mucus may be coughed up or there may be a slight hemorrhage. In some cases there may be stupor and death may occur from syncope. Where liquid preparations containing chlorine have been taken, the gastro-intestinal symptoms are noted, as a result, probably, of the irritation from the alkali of which such fluids are largely composed, together with the above signs of respiratory disturbance.

Fatal Dose.—This is a very difficult matter to determine, as nothing is known in the reported fatal cases of the intake of chlorine. The concentration of chlorine recommended for therapeutic purposes is about 0.015 mg. per liter of air, while much larger concentrations may prevail in the industries. The effect is to be regarded as a function of the concentration of the gas times the length of exposure. According to Henderson and Haggard the maximum concentration allowable for prolonged exposure is 1 part per million; the maximum concentration allowable for exposure of ½ to 1 hour is 4 parts per million; while a concentration of 40 to 60 parts per million is dangerous for even short exposure.[1] The usual time of death may, probably, be stated as about 48 hours after the inhalation, although there is little information bearing on this subject.

Treatment.—The patient should be removed from the contaminated atmosphere and allowed to breathe fresh air as rapidly as possible. It has been recommended that either dilute ammonia vapors or hydrogen sulphide be inhaled in order to neutralize the free chlorine, but such treatment would seem to be too irritating to the affected tissues as well as even dangerous. Inhalations of steam would seem to be preferable, as this might tend to allay the irritation and persistent cough. The general symptoms should be treated as they arise.

Postmortem Appearances.—There is usually a somewhat marked inflammation of the mucous membrane of the upper, as well as the lower, air passages, with pulmonary edema and pneumonic patches scattered throughout the lung. The mucous membrane of the stomach may show irritation with some areas of ecchymosis. The kidneys, in some cases at least, show slight nephritis.

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[1] *Noxious Gases,* 1927, p. 132. See also Lehmann, Arch. f. Hyg., 1887, 7, 231.

Detection.—Free chlorine is not to be found in the tissues. It has been assumed that the moment the free chlorine comes in contact with the tissues it reacts with the moisture to form hydrochloric acid, but this would not seem to be a tenable theory, as chlorine is far more toxic than hydrochloric acid and has a much more extensive area of action than does the acid. Henderson and Haggard incline to the theory that the major factor of the action is oxidation and the later irritant action of HCl, the chlorine abstracting hydrogen from the moisture present and liberating oxygen, hydrochloric acid being then formed; while Binz believes that the free chlorine is converted into sodium hypochlorite.

The finely divided tissue is treated with water, slightly acidified with nitric acid, placed in a distilling flask, when distillation in a stream of CO_2 is carried out. Hypochlorous acid passes over in the distillate and may be recognized by the fact that free Cl is liberated on treatment of the distillate with HCl. The chlorine may then be recognized by the formation of silver chloride on passing the liberated gas into a solution of silver nitrate or by the blue color produced by it on coming in contact with an iodized starch solution. As a very sensitive test one may treat 100 cc. of the distillate with 1 cc. of a $\frac{1}{10}$ per cent. solution of o-toluidin in 10 per cent. HCl, after a few minutes a yellowish to greenish color will appear, the shade depending upon the concentration. If the concentration of Cl is greater than 3 parts in a million, more reagent must be added to obtain the best results. Quantitative values may be obtained by comparison of the color with that of standard solutions.[1]

BROMINE

This halogen finds frequent use in chemical technology and, also, occasionally in sanitary work as a disinfectant, yet the reported cases of poisoning from its use are relatively few. Witthaus was able to find, up to 1911, only 5 instances of bromine intoxication, two of which were suicidal, 1 either accidental or homicidal, and the remaining 2 undetermined. The rather wide-spread use of the bromides has lead to some cases of poisoning, but few of these cases have proven fatal, being more frequently of the chronic type. During the World War liquid bromine was used in hand grenades and caused much suffering and many deaths from asphyxiation.

Properties.—Bromine is a dark, reddish-brown liquid, which vaporizes in dense red fumes, which have a very pungent and irritating odor. It is readily soluble in water to the extent of about 3 per cent. and is more soluble in alcohol, ether, carbon disulphide, and chloroform. Chemically it has great similarity to chlorine but is less energetic in its reactions. While it is found in marine plants and animals, it does not seem to be a normal constituent of the human tissues, although Damiens[1] reports the presence of less than 1 milligram per 100 grams of tissue. The bromides of ammonium, calcium, sodium and potassium are official, while several organic bromine derivatives are either official or are found in New and Non-Official Remedies.

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[1] See Ellms and Hauser, Jour. Ind. & Eng. Chem., 1913, **5**, 915.

Symptoms.—If the vapor of bromine be inhaled, there are symptoms of violent irritation of the air-passages, associated with salivation, sneezing, cough, spasm of the glottis, sense of suffocation, pain in the chest, and later bronchitis and signs of pneumonia. There may be such general symptoms as dizziness, headache, and some stupor, followed by collapse. If swallowed, it produces marked irritation of the throat, esophagus and stomach, resulting in pain in these regions, vomiting of bromine-containing material, swelling of the mouth and esophagus and a yellowish-brown coloration of the tissues. Later diarrhea, dizziness, stupor, collapse and death may follow. Applied locally to the skin, as in the use of the liquid form during war, the skin is stained brownish, from formation of brom-substitution products, and may show the appearance of vesicles followed by necrosis. The vapors in such cases may be so concentrated that death may result rapidly from suffocation, or, if the victims survive, severe conjunctivitis and inflammation of the air-passages may supervene.

The long-continued use of the bromides, and even very large single doses, produce certain exaggerations of their usual therapeutic effects in that the symptoms are much more severe. There may be noted an odor of bromine on the breath, mental apathy, nervous depression, muscular weakness, tremors, vertigo, and collapse. In many of these cases a severe eruption, *acne bromica vegetans* or *bromoderma*, may be observed. Dillingham and McCafferty[2] have recently reported a bromide eruption on the hard palate, which is the third case reported of such an eruption on the mucous surfaces, the other two being upon the tongue.

Fatal Dose.—Probably the smallest fatal dose reported is that of 0.203 gram, which was given to a child of ten years[3]; while in an adult 1 ounce[4] has proven fatal. Eigner[5] has reported the death of a woman, who had increased her dosage of potassium bromide until this amounted to two teaspoonsful (120 grains) daily, which was continued for several weeks when severe symptoms appeared and death ensued.

Fatal Period.—In Snell's case, mentioned above, death occurred in 7½ hours, while death in other cases has been deferred for six days.

Treatment.—For the irritation of the throat and air-passages, inhalation of ammonia vapors and the washing out of the mouth with mucilaginous drinks may prove of value. If the bromine be swallowed, the stomach should be evacuated and washed out with mucilaginous fluids containing starch or albuminous substances. Kobert recommends the use of alkalies to combat the action of the HBr, which is formed in the tissues affected. Wile[1] advocates the use of intravenous injections of physiologic sodium chloride solution in bromide intoxication in order to liberate bromine from the tissues and insure its liberation by way of the kidneys.

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[1] Bull. Soc. Chim. Biol., 1921, **3**, 95.

[2] Jour. Amer. Med. Assoc., 1928, **90**, 845.

[3] Hering, Ztschr. f. Med.-Beamte, 1889, **2**, 217.

[4] Snell, New York Med. Jour., 1850, **5**, 179.

[5] Wien. med. Presse, 1886, **27**, 815.

Postmortem Appearances.—The tissues attacked may show a yellowish-brown color. The larynx and trachea may show all stages of inflammatory change, even up to the formation of false membranes. The stomach may be markedly eroded, showing ecchymotic spots, or, as reported in one case, the stomach may be partially destroyed, appearing as if burnt, while the intestines may have the appearance of being cooked.

Detection.—Although in some of the postmortems reported, the tissues have smelled strong of bromine, it is probable that free bromine is rarely to be found, but, rather, hydrobromic acid and brom-protein compounds. If the presence of bromides can be excluded as the cause of the poisoning, and this is usually possible from the appearance of the tissues, the detection of the bromine ion is all that is necessary to prove the case as one of bromine poisoning, as the amount of bromine ions in the tissues normally, if any actually exists, is too small to interfere with such conclusions. In the case of bromide poisoning, Wile and his co-workers have shown that ingested bromide is excreted with difficulty by the urine and, in consequence, is stored up in the tissues of the body, the bromide replacing the chloride of the body. Vilén[2] has reported the distribution of bromine in a case of fatal sodium bromide poisoning, finding the greatest amounts in the cerebral cortex, lungs and kidneys, in which organ it varied between 0.3 and 0.5 per cent.

If the organ or stomach contents smell suggestive, it may be possible to obtain free bromine by distilling the finely divided tissue, after mixing with water, but this is rarely advisable. Probably the best procedure is the following: Treat the finely divided tissue, stomach contents, urine, blood, or other material, with a solution of potassium hydrate, evaporate to dryness, carbonize and incinerate. Take up this residue with water, place in a distilling flask, add a little potassium dichromate and strongly acidify with dilute sulphuric acid. Distill the mixture, using a very cold condenser, when free bromine will pass over with the aqueous vapor. To this distillate the usual qualitative tests for bromine may be applied.

In cases of suspected bromide poisoning, the urine may yield direct evidence if tested as follows, according to Jolles. Place 100 cc. of urine in a narrow-necked flask, acidify with sulphuric acid and add a solution of potassium permanganate until the color of the mixture is distinctly red. Suspend in the neck of the flask a piece of filter paper moistened with a 1:1000 aqueous solution of para-dimethylphenylenediamine and warm the mixture on the water-bath. In the presence of traces of liberated bromine, characteristic color rings will appear on the paper, the inner ones of a violet tone, while the borders show tints of blue, green or brown. For this same purpose Belote[1] recommends a modification of a test given by Fresenius[2], using, instead of the reagent of Jolles, filter paper impregnated with a solution of fluorescein and moistened with dilute acetic acid, when a bright pink or red color will appear on the test paper in the presence of bromine to the extent of 1:50,000.

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[1] Arch. Dermat. & Syph., 1922, **6**, 529; Ibid., 1923, **8**, 407; Jour. Amer. Med. Assoc., 1927, **89**, 340.

[2] Upsala Läkareför. Förhandl., 1926, **31**, 373; Abs., Jour. Amer. Med. Assoc., 1926, **87**, 2136.

IODINE

Iodine is rather widely distributed in nature, being found in sea-water, in many salt deposits, in marine animals and plants, and in the vertebrates, especially located in the thyroid gland but present, also, in many other organs[3] in organic combination. On account of its wide use in chemistry and, in various forms, in medicine, iodine and its preparations have lead to quite a few cases of poisoning, either from inhalation of its vapors or from the administration of its solutions, or the application of its liquid preparations to the skin or abraded surfaces. Witthaus, up to 1911, found in the literature 31 cases of poisoning with iodine and its preparations, 20 of which were accidental, 9 were attempts at suicide, and 2 were unsuccessful efforts at homicide. In New York City in the years 1918 20, there were 1 accidental and 4 suicidal cases, while in Chicago during the same period there were 1 accidental and 1 suicidal cases.

Properties.—Iodine occurs as a heavy, bluish-black, brittle, crystalline substance, occurring in rhombic plates having a metallic luster and a distinctive, irritating odor. It is not readily soluble in water, requiring 2950 cc. of water to dissolve 1 gram, while it is readily soluble in alcohol, glycerin, carbon disulphide, chloroform, carbon tetrachloride, ether, aqueous solutions of iodides, and paraffin oil. It volatilizes slowly at ordinary temperatures, but rapidly at higher ones. It is official in the form of the *Liquor Iodi Compositus* (Lugol's solution containing 5 per cent. free I dissolved in 10 per cent. KI), *Tinctura Iodi* (containing 7 per cent. I and 5 per cent. KI in alcoholic solution), and the *Unguentum Iodi* (containing 4 per cent. free I and 4 per cent. KI in a mixture of glycerin and wool fat). Its salts recognized by the Pharmacopoeia are Arsenous Iodide, Liquor Arseni et Hydrargyri Iodidi, Hydrargyri Iodidum Flavum, Hydrargyri Iodidum Rubrum, Potassium Iodide, Sodium Iodide, Syrupus Ferri Iodidi, and Thymol Iodide; while in organic combination Calcium Iodobehenate is official.

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[1] Cited by Wile, *Loc. cit.*, p. 340.

[2] "Qualitative Chemical Analysis", 17th ed., 1921, p. 450.

[3] See Maurer, Ducrue and Palasoff, Münch. med. Wchnschr., 1927, **74**, 271.

Symptoms.—Applied to the skin, iodine produces a brownish stain and, in some cases, a desquamative dermatitis, which may occasionally become purulent. When inhaled, in the form of its vapor, it produces marked irritation of the upper air passages and may produce sudden collapse and death. Taken internally, in the form of the tincture or Lugol's solution, it colors brown the mucous membranes of the mouth, esophagus, and stomach, pain in the mouth and stomach, vomiting of brownish or of bluish material (if starch be present in the stomach), purging, weak pulse, delirium, stupor, and collapse. The urine may show albumin and blood, along with other evidences of irritation. Occasionally the urine may be almost suppressed. If applied to abraded surfaces or injected into various cystic cavities, it produces general disturbances, such as headache, dizziness, delirium and collapse, and at the same time gastric irritation may be observed.

When taken in the form of the iodides, over a long period or in very large doses, the symptoms of "acute iodism" may be observed. These usually begin with a metallic taste in the mouth, salivation, sneezing, coryza, conjunctivitis, then follow stomatitis, bronchitis, supraorbital neuralgia, circulatory disturbances, etc. Probably the most common sign of irritation from the iodides is the appearance of eruptions on the skin, which may take the form of acne, urticaria, or, occasionally, of pemphigus.

Fatal Dose.—From experiments on rabbits Holm[1] concluded that the size of the dose is not the only factor that influences the severity of iodine poisoning. Other things to be considered are the behavior of the thyroid, the factors which liberate iodine in the body[2] and the reaction of the tissues to the free iodine. He believes that it is not possible to state a definite lethal dose for the human being, as it may be under 0.2 mg. or more than 43.6 grams per day. The smallest dose taken internally, which has been known to have caused death of an adult, appears to be 1 dram (3.9 grams)[3]; while in a child it is 20 grains[4](1.3 grams). Probably the average fatal dose may be taken as 3 to 4 grams of free iodine. Of the tincture the fatal dose probably averages 1 to 2 fluidrams, but recovery has occurred from doses of 1 fluidounce. With the potassium and sodium iodides, the fatal dose is rather indefinite, as there have been few fatal cases. In one case reported by Wolf[5], death occurred in 8 days after taking 6 grains four times in 1 day, but this can not be taken as an average case as there were renal and cardiac diseases present at the time.

Fatal Period.—Death may occur in 24 or 48 hours, or may be delayed for several days.

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[1] Dermatol. Wchnschr., 1926, **83**, 1796.

[2] See Kobert, *Lehrbuch der Intoxikationen*, 2nd ed., 1906, **2**, 184.

[2] Jackson, Prov. Med. Jour., 1847, p. 356.

[4] Gairdner, *Essay on the Effects of Iodine*, 1824, p. 20. Cited by Witthaus.

[5] Berlin klin. Wchnschr., 1886, **23**, 578.

Treatment.—Administration of starchy fluids, either in the form of the ordinary household starch, or as gruels of rice, barley, etc., should be prompt and frequently repeated. Vomiting should be induced or the stomach should be frequently washed out with such starch fluids. Instead of these measures, one may wash the stomach with a 5 per cent. solution of sodium thiosulphate, in order to convert the free iodine into sodium iodide. The symptoms should be combated as they arise. Alkalies should be administered to prevent the liberation of free iodine in the tissues.

Postmortem Appearances.—Marked irritation and inflammation of the mucous membrane of the mouth and esophagus will be observed, and some edema of the glottis may be present. The mucous membrane of the stomach and intestines may be swollen and stained yellow-brown, and some areas of corrosion may be noted. The heart, liver and kidneys may show fatty degeneration, or the kidney may be the seat of a distinct glomerulonephritis.

Detection.—Iodine is eliminated from the system in the various excretions and is found especially in the stomach contents, contents of the intestines, urine, saliva, sweat, etc. While in most of the cases free iodine is not found in the urine, yet this has been detected in some cases[1]. When iodine comes in contact with albuminous tissues or fluids, it is bound partly by the alkali and partly by the protein. In the blood it is converted largely into the form of sodium iodide, and is excreted as such.

To detect the presence of free iodine, the tissues, mixed with water, are distilled, the vapor being condensed in a very cold condenser. If there is sufficient free iodine, the distillate may be colored yellowish or even violet. If the color is not suggestive, the usual qualitative tests may be applied.

If no free iodine is present, add potassium hydroxide and sodium nitrate and evaporate to dryness in a silver crucible. Incinerate at as low a temperature as possible, extract the ash with alcohol, filter, evaporate the filtrate to dryness and take up the residue with water. Transfer this solution to a distilling flask, acidulate with sulphuric acid and add some potassium dichromate and distil. The distillate will contain any iodine which existed in the tissues in metallic combination. Qualitative tests are applied to this distillate. Quantitative estimation may be carried out by precipitation of the iodine as palladous iodide and weighing as such.

In determining the presence of iodides in the urine, one may evaporate the urine with sodium hydroxide as above outlined. Or, the following procedure may be followed. Acidify the urine with sulphuric acid, add a few cc. of solution of sodium or potassium nitrite, and shake the mixture with chloroform or carbon disulphide, when the free iodine will pass into solution in the immiscible solvent. Qualitative tests may then be applied. Should one wish to determine the amount of iodine in the urine, the process of Marsh[1] yields reliable results. This method consists of the preliminary determination of the total halogens in the residue from a fused sample of urine by the usual Volhard-Arnold technic, and, then, the determination of the chlorides in another fused sample from which the iodine has been removed by boiling with sulphuric acid and sodium nitrite solution. The difference between these values yields the iodine present in the amount of tissue taken.

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[1] See Hermann, St. Petersb. med. Wchnschr., 1868, **15**, 336.

FLUORINE

Fluorine is found in nature in the form of fluospar and cryolith, in plants, in milk and eggs, and in almost all tissues of the human body, especially in the teeth and bones.[2] In the form of sodium fluoride and sodium fluosilicate it has been used as a preservative of foods and drinks and as an insecticide, the latter containing from 15 to 65 per cent. of sodium fluoride. While there have not been deaths reported, Witthaus cites 3 cases of suicide from hydrofluoric acid, while sodium fluoride has caused accidental death in several cases[3] and a few deaths[4] from sodium fluosilicate have been reported.

Properties.—Free fluorine is so seldom found, that it needs only mere mention. It is a very irritating gas, which, when breathed and coming in contact with the moisture of the tissues, decomposes the water with formation of hydrofluoric acid and ozone. Hydrofluoric acid, HF, is a colorless gas, which is very soluble in water and imparts to it a fuming, very irritating and corrosive power. The sodium fluoride is a white powder crystallizing in cubes, has an acrid bitter taste, and is soluble in about 25 parts of water, while the sodium fluosilicate is even less soluble.

Symptoms.—The action of the fumes of hydrofluoric acid is practically the same as noted with hydrochloric acid. Severe pain in the throat and stomach, vomiting, and collapse are commonly observed, death usually being very rapid. The salts of this acid exert their irritant action through the liberation of fluorine, which combines with the calcium of the tissues and becomes, therefore, a protoplasmic poison.[5] Taken into the stomach, nausea, vomiting, purging, and symptoms of corrosion may appear, although some cases do not show any gastro-intestinal symptoms. Later, there may develop muscular and cardiac weakness, edema, neuralgia, loss of speech, and signs of renal irritation.

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[1] Jour. Lab. and Clin. Med., 1923, **8**, 271.

[2] See Kickton and Belinke, Ztschr. f. nahr. u. Genüssmit., 1910, **20**, 193; Zdarek, Ztschr. f. physiol. Chem., 1910, **69**, 127; Gautier, Compt. rend. Acad. d. sci., 1913, **156**, 1425.

[3] See Baldwin, Jour. Amer. Chem. Soc., 1899, **21**, 517; Hickey, Bull. Mass. Board of Health, 1911, p. 341; Report of the Chief Medical Examiner of the City of New York, 3 accidental deaths in 1918–20, 2 accidental deaths in 1925, and 1 accidental and 1 suicidal death in 1926; McNally, Jour. Amer. Med. Assoc., 1923, **81**, 811, who reports 3 accidental and 1 suicidal death in Chicago.

[4] See Sommelet, Bull. sci. pharmacol., 1923, **30**, 211; Kurtzahn, Deutsch. med. Wchnschr., 1923, **49**, 319; Lührig, Chem. Ztg., 1924, **48**, 613; Ibid., 1926, **50**, 593.

[5] See Wieland and Kurtzahn, Arch. exper. Path. und Pharmacol., 1923, **97**, 489.

Fatal Dose.—In one case death has resulted from swallowing 15 cc. of hydrofluoric acid in solution[1], while another case[2] is reported of death from taking about a tablespoonful of 9 per cent. acid diluted with water. According to Baldwin[3] 5 grams of sodium fluoride would cause toxic symptoms and 10 grams would prove fatal.

Fatal Period.—Death has occurred in 35 minutes from hydrofluoric acid, while in the cases of sodium fluoride poisoning death occurs in most cases in from three-quarters[4] to 4 hours, although some are prolonged to ten to twelve hours, and a child has died in 5 minutes from a dose of fluosilicate.[5]

Treatment.—As the sodium salts of hydrofluoric acid are rather difficultly absorbed from the stomach and bowels, solutions of lime water and calcium chloride should be used as fluids for gastric lavage in order to convert the acid or the slightly soluble sodium salts into the insoluble calcium compounds. The portion of the sodium salts that has been absorbed is rapidly converted into the calcium salt in the tissues and stored up especially in the bones, elimination taking place rather slowly. Symptomatic treatment should be given as occasion demands.

Postmortem Appearances.—The mucous membrane of the mouth, throat, stomach and intestines shows inflammatory and ulcerative changes similar to those noted with hydrochloric acid. The kidneys may show evidences of nephritis. Crystalline deposits of calcium fluoride may be found in the liver, kidneys and other organs.

Detection.—Owing to the presence of fluorine in small amounts in certain tissues, the finding of a trace of fluorine is not to be regarded as evidence of poisoning. The presence of this halogen may be detected by adding to the suspected tissue some solution of sodium hydroxide and incinerating the mixture. Treat the ash with concentrated sulphuric acid and warm in a platinum dish, covered with a watch-glass, which has been coated with paraffin on its under surface. If a design or a word be scratched in the paraffin coating, the glass will be found to be etched in this form if fluorine be present in the residue. If silica be present in the material under examination, this test may prove negative, as silicon fluoride is formed, which does not corrode glass. Under these circumstances, a glass rod wet with water and held over the crucible evolving the gas will show a film of silicic acid, which indicates the presence of silicon fluoride in the gas evolved. Quantitative determination is made by incinerating the hashed tissue with sodium hydroxide and the estimation of the fluoride present by precipitation as calcium fluoride in the usual manner.

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[1] King, Trans. Path. Soc. London, 1873, **24,** 98.

[2] Stevenson, Brit. Med. Jour., 1899, **2,** 1145.

[3] *Loc. cit.*

[4] McNally, Jour. Amer. Med. Assoc., 1923, **81,** 811.

[5] Lührig, Chem. Ztg., 1924, **48,** 613.

PHOSPHORUS

Phosphorus is found as a constituent of the tissues and fluids of the human body, being especially important in the bones and in the phospholipins of the nervous tissues and blood as well as in the nucleo-proteins. It has been widely used to tip matches and as a constituent of rat and mice paste, and, as a result, has been frequently employed in cases of poisoning. The amount of phosphorus in the paste used in making match heads varies to a great extent, but it may be considered that it runs from 0.3 to 2 mg. per match. The paste used for rat poison varies from 1 to 4 per cent. of phosphorus. At the present time the use of yellow phosphorus in matches has been greatly curtailed, so that poisonings are far less frequent. In 1911 Witthaus[1] was able to find records of 802 cases of poisoning by phosphorus, in only 26 of which was the substance taken in a form other than as match heads or vermin poison.[2] Of these cases 123 were homicidal, 388 suicidal, 88 accidental, 67 taken to produce abortion, 1 tried as an experiment, 2 used by quacks, and the remaining 133 were of unknown origin. Although the use of yellow phosphorus has been largely eliminated by legislation in various countries and the red non-poisonous form substituted, yet several deaths of children have recently occurred from eating fireworks, especially of the type of the "spit devil", such preparations containing several per cent. of yellow phosphorus.[3] A few cases of poisoning have occurred from taking overdoses of medicinal preparations containing phosphorus, especially phosphorized cod-liver oil.

Properties.—The ordinary form occurs as a translucent, nearly colorless solid, having a waxy luster, and a consistence at ordinary temperatures about that of bees-wax. When kept under water it turns yellow, and, after long keeping the surface becomes white or red, and occasionally black. It has a distinctive odor resembling that of garlic. It is practically insoluble in water, only about 0.2 mg. dissolving in 100 grams of water, although the water assumes the characteristic garlic-like odor and taste. One gram of phosphorus is soluble in about 400 cc. of dehydrated alcohol, in about 40 cc. of chloroform, 102 cc. of absolute ether, 31.5 cc. of benzene, and 0.9 cc. of carbon disulphide, at 25°C. It is sparingly soluble in fixed oils but quite readily in volatile oils. On exposure to the air, phosphorus emits white fumes of its oxides, these fumes being luminous in the dark. On longer exposure to the air, it often takes fire spontaneously. The official preparation of this yellow phosphorus is the Pilula phosphori, which contains 0.6 mg. ($^1\!/_{100}$ grain). An allotropic form, known as *red phosphorus*, is now used almost entirely in the manufacture of matches, as it is, in itself, non-poisonous and does not oxidize in the air. However, it should be recalled that occasionally some samples of this red phosphorus may contain a small percentage of the true waxy type and may, therefore, cause toxic symptoms; while, if the pure red phosphorus finds its way into the tissues, especially in experimental ways, instead of being taken by mouth, it may itself produce mild toxic symptoms.[1] In the manufacture of matches, some "lucifer" matches are still tipped with a paste of waxy phosphorus mixed with potassium chlorate, sand and glue, but the use of this form of phosphorus is fast disappearing, many manufacturers substituting phosphorus sulphide (P_4S_3), or, preferably, tipping the so-called "snapping" matches with a paste of red phosphorus, potassium chlorate and glue. In the case of the "safety" matches, the match head is tipped with a paste of potassium chlorate and sulphide of antimony, while the side of the box upon which the match is struck is coated with a paste of red phosphorus, sand and glue.

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[1] *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 1911, **4**, 636.

[2] See McLean, MacDonald and Sullivan, Jour. Amer. Med. Assoc.,1929, **93**, 1789.

[3] See Stacy, Jour. Amer. Med. Assoc., 1921, **77**, 1514; Corwin, New York State Jour. Med., 1922, **22**, 475; Dwyer and Helwig, Jour. Amer. Med. Assoc., 1925, **84**, 1254.

ACUTE POISONING

It is probable that the deleterious effects of phosphorus are evident only when it is in the elementary form or in combination with hydrogen, as its oxygen compounds seem practically inert, except in so far as the acids may exert some local corrosive effect. As Kobert[2] remarks: "The danger of poisoning is practically over, if the organism has oxidized the phosphorus only up to the stage of the suboxide or to hypophosphorous acid. However, this oxidation proceeds more slowly and more difficultly than one would think." This slow oxidation in the body is shown by the fact that phosphorus remains unoxidized in the circulating blood for some time and does not reduce the oxyhemoglobin to methemoglobin. Moreover, it retards the normal oxidative metabolic process of the system. Apparently phosphorus itself has no local irritative effect on the stomach, this organ being secondarily affected during the process of elimination rather than primarily during absorption, although vomiting and gastric pain are early symptoms and some cases of rapid death do show evidences of lesions in both stomach and bowels. Elementary phosphorus is absorbed as such in sufficient quantities to produce fatal results even from aqueous and alcoholic liquids, this absorption being facilitated by the presence of bile and, especially, of oily and fatty material, but in most cases the process is slow and the appearance of symptoms is delayed, as a rule, from 2 to 6 hours. Under the influence of the absorbed phosphorus, the number of the red cells of the blood is increased and the degree of alkalinity is diminished, while the normal synthetic processes are retarded and autolytic decompositions facilitated.

Symptoms.—Soon after ingestion of the phosphorus-containing material, the patient may complain of the garlic-like taste, but there is usually a variable interval before symptoms of the toxic action appear.

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[1] See Kobert, *Lehrbuch der Intoxikationen*, 2te. Aufl., 1906, **2**, 290.

[2] *Ibid.*, p. 287.

To be most effective the phosphorus must be either in solution or finely divided in the form of an emulsion in fatty material. If taken in large pieces, the effect is much slower and by no means commensurate with the amount taken. As a rule, the time after ingestion before symptoms appear is 2 to 6 hours, but in rare cases these may appear almost at once or, in others, be delayed for a period of 12 to 48 hours. The patient complains of pain and burning sensations in the throat and stomach, accompanied with eructations of gas with a garlic-like odor and then by vomiting of material which smells strong of garlic, and may emit light (phosphoresce) when in the dark. The breath in this stage may be luminous in the dark and the mouth and lips may show this phosphorescence from the adherence of particles of phosphorus to the mucous membrane. There may be rather severe purging in this stage, the fecal material often showing this same phosphorescence. This stage of acute irritation does not ordinarily last longer than 1 to 2 days, although occasionally it may continue much longer[1], while in other cases there may be only one act of vomiting with a fatal result 12 hours later[2]. Occasionally, in this stage, the symptoms are so severe that death has resulted from collapse and cardiac paralysis.

Following this irritative period, there is usually an abatement of the symptoms and a period of comparative comfort, or euphoria, the patient so far recovering as to seem practically well for some days or even weeks, although in some cases the so-called second stage follows promptly. There now appears jaundice which increases in depth and severity with the intensity of the poisoning, associated with a recurrence of the symptoms first noted. The vomiting may be almost continuous and the purging may be marked, both discharges being bloody. Gastric pain may be marked, there is tenderness over the liver, and an increased area of hepatic dulness appears, which may be followed, later, by a diminution. The tongue is furred and the breath fetid. In some cases hemorrhages may occur from various mucous membranes, as from the nose, mouth, bladder, uterus and vagina, and abortion may occur in women who are pregnant. Frontal headache may be severe, sleeplessness, a feeling of anxiety, and cramps in the legs and arms may be noted, and itching eruptions of the skin may appear. The pulse is at first of normal frequency but soon becomes weak and rapid, while the respiration is shallow and rapid. Lawrence and Huffman[3] call attention to an increase in the number of monocytes in the blood. The urine shows evidence of the poisoning in the dark color due to bile pigments, the presence of albumin, hyaline and fatty casts, free fat droplets, blood cells, lessened urea content, and the presence of amino acids, especially of leucin and tyrosin, although glycine, alanine, arginine, and others have been found. It should be mentioned, however, that these amino acids are not always found. The blood sugar is reduced, while the blood nonprotein nitrogen is slightly increased, of which the amino-acid nitrogen forms a very large percentage[1]. There may be marked muscular weakness, which may involve the heart with resulting cardiac failure. In many cases delirium, convulsions, coma, syncope, paralyses, etc. may occur. Death may occur at any stage of the poisoning, depending, of course, upon the severity of the early symptoms, which may lead to collapse, or upon the later effects upon the liver and kidneys, which may prolong life for a week or more. It should be mentioned that the symptoms of phosphorus poisoning and of acute yellow atrophy of the liver are very similar, the only reliable means of differentiation being the detection of unoxidized phosphorus in the excreta or vomitus, although the rapid enlargement of the liver in the former as compared with the diminution in the latter and the more frequent association of cerebral symptoms with acute yellow atrophy should offer some hope of differential diagnosis.

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[1] See Roque and Dumas, Provence med., 1907, **18**, 430, who report a case in which the primary gastro-enteric stage lasted for 15 days, and was followed by a period of sedation of 3 weeks.

[2] See Casper, *Handbook of Forensic Medicine*, New Sydenham Society Edition, 1862, **2**, 100.

[3] Arch. Path., 1929, **7**, 813.

Fatal Dose.—Probably the smallest fatal dose for a child is that cited by Sonnenschein[2] of death of a child five weeks old as a result of swallowing the head of a single match (about 2 mg.), while in Franke's case of death of a child of two years the fatal dose was 3 mg. of phosphorus in cod-liver oil.[3] In the adult the fatal dose is difficult to determine, as the toxicity depends to a great extent on the state of subdivision of the phosphorus and the possibilities of absorption, as well as upon individual peculiarities, individuals who are the subject of nervous diseases probably being somewhat more susceptible.[4] Death has occurred from the taking of match heads estimated to contain 0.065 to 0.13 gram (1 to 2 grains) of phosphorus,[5] while recovery has followed the taking of the heads of 2000 matches along with the hot water in which they had been macerated, representing probably, between 2 and 3 grams.[6] It is probable that a dose of 0.05 to 0.06 gram (¾ to 1 grain) would produce decidedly dangerous or fatal symptoms in a healthy adult.

Fatal Period.—The time of death in phosphorus poisoning has varied greatly in the reported cases, the range being from a period less than 1 hour to a week or more. Habershon[7] refers to a case of Dr Tüngel of death in ½ hour, while Taylor[1] states that Orfila mentions a death in 4 hours. Witthaus[2] believes that these cases are not authentic as he states that the "shortest duration was 7 hours in a case reported by Jäderholm."[3] He further says that "Among 251 fatal cases in which the duration was accurately reported, 36 died during the first day; 209 in a period varying from 2 days to 2 weeks (19 in 2 days; 32 in 3; 41 in 4; 33 in 5; 29 in 6; 23 in 7; 7 in 8; 9 in 9; 5 in 10; 4 in 11; 5 in 12; and 2 in 14 days), the average duration being 5¼ days, and 6 in longer periods."

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[1] McLean, MacDonald and Sullivan, Jour. Amer. Med. Assoc., 1929, **93**, 1789.

[2] *Handbuch der gerichtlichen Chemie*, 1869, p. 23.

[3] Virchow's Jahresber., 1901, **36**, 617.

[4] Holland in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 149, cites an observation of Lobel of the death of an insane patient from a dosage of 7.5 mg. (0.116 grain).

[5] Lamprecht, Friederich's bl. f. ger. Med., 1868, **19**, 243.

[6] Blaschko, Vrtljschr. f. ger. Med., 1877, **27**, 563. For other similar cases but with less amounts involved see Singer, Prag. med. Wchnschr., 1883, **8**, 509; and Vogt, China Med. Jour., 1924, **38**, 123.

[7] Med.-Chir. Trans., 1867, **50**, 92.

Treatment.—In every case in which there is suspicion of phosphorus poisoning, the treatment should be begun at once instead of waiting for the symptoms to develop, as these may be delayed for some hours. The stomach should be evacuated at once by means of the stomach tube and gastric lavage should be conducted with a solution of about 1 per cent. potassium permanganate, this process being frequently repeated. As the permanganate is reduced by the organic substances of the food, it must be given in excess and frequently repeated, but the solution should be no stronger than a 1 per cent. solution in order to avoid unnecessary gastric irritation. Instead of the permanganate, a 1 to 3 per cent. solution of hydrogen peroxide may be employed. After the lavage, a cathartic should be administered and the bowel should be flushed with high colonic irrigation of warm water followed by a dilute solution of potassium permanganate. This treatment will remove much of the phosphorus present in the bowel. Following this old ozonized turpentine should be given in doses of ½ teaspoonful in mucilaginous emulsion several times daily and continued for several days. Sodium bicarbonate should be given freely in order to increase and maintain the alkalinity of the blood, which has been decidedly lowered by the action of the phosphorus. All substances containing fats and fixed oils should be avoided in the diet in order to prevent rapid absorption of the phosphorus from the gastro-intestinal tract, although Atkinson[4] believes that liquid petrolatum may be used as an unabsorbable solvent for the free phosphorus. Symptomatic treatment should be followed as occasion arises.

Postmortem Appearances.—It is clear that the postmortem changes will vary with the duration of the poisoning. In the very acute cases the findings are almost negative with the exception of cloudy swelling of the mucous membrane of the stomach, of the heart muscle, of the liver and kidneys, but the presence of phosphorus may be detected in the stomach and intestinal contents. If the poisoning has continued for two days or more, the signs of degeneration in the large glandular organs and the heart are well developed, while if death does not occur for 3 to 5 days, the signs are especially characteristic. Here we find the skin yellow and often marked with hemorrhagic spots of variable size. The internal organs are slightly icteric and the parenchymatous organs show a high-grade fatty degeneration. Absence of jaundice is ordinarily noted in those cases of short duration and in rare cases of longer duration than two days. The extravasations of blood, either in the form of small petechiae or of larger ecchymoses, may be noted in the pleurae, pericardium, mediastinum, in the subcutaneous tissue, in the muscular tissue, lungs and mesentery[1]. In the female, hematomata are occasionally found in the ovaries, and the uterus may be much congested. The stomach may be congested, the mucous membrane swollen and softened, while the chief cells of the peptic glands may show a high-grade fatty degeneration, so that even by microscopic examination the mouths of the glands appear in the form of yellow points (the so-called *gastroadenitis phosphorica* of Virchow), while the mucous membrane may show small erosions. The liver is practically always enlarged, although in a very few cases it has been reported as normal in size or somewhat smaller. It is saffron-yellow in color, with occasional red spots, while it is rather pulpy in consistence. The cut surface is yellow and very greasy, the acini being large and easily recognized. Microscopic examination shows marked fatty degeneration, the accumulation of fatty globules in the Kupffer cells being an early manisfestation[2]. The kidneys are larger in size than normal, icteric in color, and of a very soft consistence. Their cut surface is yellow and greasy, while microscopic examination shows marked fatty degeneration. The muscular tissue, as well as the heart muscle, shows, also, a high-grade fatty degeneration. Degenerative changes may be found, also, in the brain and spinal cord, and, occasionally, small hemorrhagic areas may be noted.

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[1] *On Poisons* 3rd Amer. Ed., 1875, p. 279.

[2] *Medical Jurisprudence, Forensic Medicine and Toxicology,* 2nd ed. 1911, **4**, 640.

[3] Hygiea, 1873, **35**, 12.

[4] Jour. Lab. & Clin. Med., 1921, **7**, 148. See, also, Dwyer and Helwig, Jour. Amer. Med. Assoc., 1925, **84**, 1254.

CHRONIC POISONING

This type of poisoning is relatively rare in these days, owing to the more limited use of yellow phosphorus in the match industry and the substitution of red phosphorus or of phosphorus sulphide. Workers in factories, where the inhalation of phosphorus fumes is possible, become the victims of so-called "Lucifer disease", "phosphorus necrosis" or "phossy jaw". "After several weeks or months obstinate toothache is felt, and when the tooth is extracted the gum does not heal, but retracts, leaving a suppurating bony surface. Pieces of bone come away, and the disease process in the marrow and in the periosteum spreads to new areas, other teeth and their sockets become involved, and greater portions of bone necrosed. Accompanying the local mischief, partly caused by it and also aggravating it, is a general disturbance of health characterized by anemia, pallor, weakness, hectic fever, diarrhea, septicemia, purpura, sometimes ending in death by exhaustion. These symptoms may be prevented by dental inspection of workmen and filling of all carious spots on the teeth, by the circulation of fresh air, by the frequent and systematic use of mouth-washes of sodium bicarbonate, and by the prompt exclusion of any one showing significant symptoms. A milder form of chronic poisoning than the necrosis of the jaw is often encountered, the symptoms of which are anemia, slight jaundice, cachexia, albuminuria, and, later on, chronic bronchitis, enteritis, and fragility of the bones."[1]

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[1] See Kobert, *Lehrbuch der Intoxikationen*, 2te. Aufl., 1906, **2**, 295, Hofmann-Haberda, *Lehrbuch der gerichtlichen Medizin*, 11te. Aufl., 1927, p. 856.

[2] Lawrence and Huffman, Arch. Path., 1929, **7**, 809.

Detection.—While the odor, taste and luminosity of phosphorus are of special interest in toxicology, yet none of these factors is to be absolutely depended upon in any given case. The taste and odor may be readily masked by substances with strong tastes or odors, while the luminosity may be prevented by the presence of many substances, of special importance being alcohol and turpentine, either of which may be present in the stomach contents during or after treatment of a case of poisoning. Phosphorus may remain in the body in the elementary form for some time, both before and after death, so that the possibility of its detection is always present. On the other hand, examination has not infrequently failed to reveal its presence in relatively rapid death from undoubted phosphorus poisoning.[2] As phosphorus exists in the body in the form of phosphates and as organic phospholipins and nuclein compounds, and is, also, present in such forms in various food products, it follows that the detection of such compounds has no value. In order to afford any evidence of poisoning, phosphorus must be found either in the elementary form or in such lower oxidation forms as hypophosphorous or phosphorous acids, although, in the latter cases, it must be remembered that both of these compounds are not infrequently used as therapeutic agents. Further, it should be mentioned that there is a possibility of obtaining volatile phosphorus compounds from the distillation of certain tissues, especially the brain and cord, so that, if these tissues are to be examined, they should be investigated separately. While the chances of detecting phosphorus are naturally greater if the tissues be examined relatively soon after death, yet phosphorus remains unoxidized for long periods in some cases, so that we find reports of its detection even after such long periods as 468 days[3] and others of somewhat less time. The organs especially important in the examination for phosphorus are the stomach and intestines with their contents, the liver, the kidneys, the brain, and, also, the blood.

Preliminary Test.—As the odor of an organic mixture is by no means conclusive evidence of the presence of phosphorus and, further, as luminosity of the organic material is not, in itself, proof of the presence of phosphorus, we employ other methods to indicate the possibility of the presence of phosphorus. Several such methods have been advocated, but probably the best of them is the Scherer[1] test. Place a little of the finely divided tissue or of the stomach contents in a small flask, add sufficient water to cover this material if enough fluid is not present, and acidify with tartaric or sulphuric acid. In the neck of this flask suspend, by means of a cork in which a V-shaped slit is cut, two strips of filter paper, one moistened with a solution of silver nitrate and the other with an alkaline solution of a lead salt[2], precautions being taken that the papers touch neither one another nor the sides of the flask. Now heat the flask to 30 or 40°C. for some time in the dark, in order to avoid the effect of light upon the silver paper. If the silver but not the lead paper be darkened in color, yellow or elementary phosphorus *may* be present; if both papers be blackened, hydrogen sulphide may be the cause or both phosphorus and H_2S may be present; but if the silver paper is not darkened, phosphorus in the free state is almost certainly *not present.* In the absence of hydrogen sulphide, blackening of the silver paper may be due to the presence of any volatile reducing agent, such as formic acid or formaldehyde, a possibility which should always be remembered in case the organs have been taken from an embalmed body. One may, of course, remove the disturbing factor of H_2S by adding to the material in the flask some cadmium sulphate before heating, but it is usually advisable to know whether or not this substance is present before proceeding with the tests to be later outlined. One may confirm the presence of phosphorus, if the silver paper be blackened, by treating this paper with *aqua regia*, evaporating the solution to dryness, taking up with water and testing with ammonium molybdate, when a yellow precipitate indicates the presence of phosphorus providing a blank test on the filter paper itself shows the absence of phosphate therein. This test of Scherer is of more value in its negative phase than in its positive phase, as a negative test excludes phosphorus, but a positive test does necessarily mean that this element is present, as phosphorus sesquisulphide, if present, will give a positive reaction.

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[1] Holland, "Inorganic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 152.

[2] See Bartschat, Ztschr. f. Nahr. u. Genussm., 1924, **47**, 10.

[3] See Bosnajakovic, Schmidt's Jahrb., 1903, **277**, 210.

Mitscherlich's Test.—This test[3] is based on the fact that yellow phosphorus volatilizes with steam and becomes luminous in contact with air. Set up the apparatus as shown in Fig. 38, taking special precautions to assure absolute cleanliness of all parts, especially the long doubly-bent tube and condenser. In the distilling flask place about 100 grams of the finely hashed organ or of the stomach contents, add sufficient water to bring the consistence of the mixture to that of a thin gruel and acidify with dilute sulphuric or tartaric acid. It is advisable to add, also, a little ferrous sulphate to eliminate the disturbing influence of oxidizing agents, which may possibly have been taken in with the phosphorus, especially if match-heads have been ingested, and some ferric chloride to prevent any hydrogen sulphide from passing over into the distillate. The flask should not be more than ⅓ full, as foaming of the material may, otherwise, carry solid matter into the tube and, thence, into the receiver. Now heat the mixture to boiling, raising the temperature gradually and employing an asbestos plate, sand bath or oil bath. The receiving flask should contain a few cc. of distilled water and the outlet tube of the condenser should dip below the surface of the water. This distillation should be conducted in a dark room free from all artificial light, the flame of the burner under the distilling flask being protected by a metal cone and a screen of black card-board placed between the distilling flask and the condenser. As the distillation proceeds, phosphorescence will be noted, in case phosphorus is present, in the long tube, being especially noticeable in the upper part of the

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[1] Ann. d. Chem., 1859, **112**, 214.

[2] Prepared by adding an excess of sodium hydroxide solution to a solution of lead acetate.

[3] Jour. f. prakt. Chem., 1855, **66**, 238.

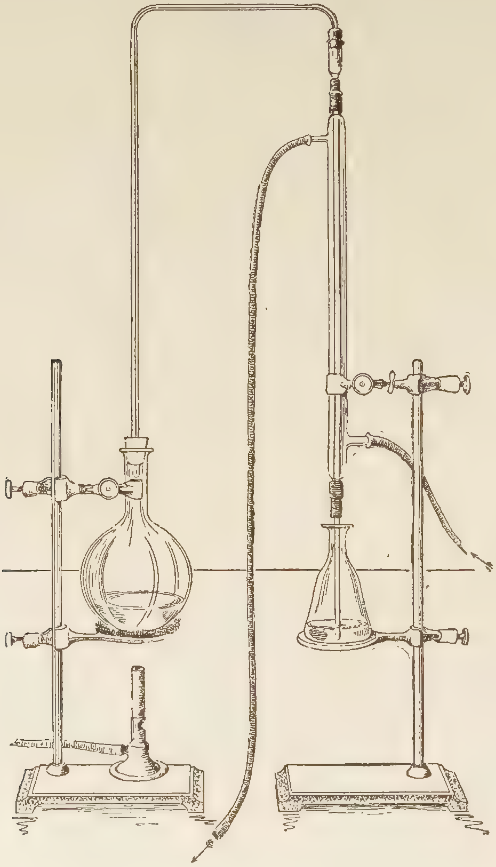

Fig. 38.—Mitscherlich apparatus. (From Autenrieth and Warren "Detection of Poisons," P. Blakiston's Son & Co., Publishers.)

condenser as a luminous ring which seems to rise and fall or as flashes of light at this point. This phosphorescence is very characteristic of phosphorus and is given by very small amounts of this element. Thus Hilger has found that 0.06–0.3 mg. of phosphorus in 200 cc. of water could be distinctly recognized, while Fresenius noted that 1 mg. gave phosphorescence which lasted for ½ hour. In this test it must be remembered that phosphorus sesquisulphide will, if present, yield this same phosphorescence, so that one may be certain of the presence of the elementary or yellow phosphorus only by the use of tests which will eliminate the sulphide.

It has been found that a large number of substances, many of which might be present in the material used for distillation, will interfere with the luminescence of phosphorus in this test. Thus, among these have been found ethyl and methyl alcohol, ether, acetic ether, benzin, ethereal oils, turpentine and other essential oils, carbolic acid and other volatile phenols, creosote, chloroform, chloral hydrate, hydrogen sulphide, ammonia, sulphur dioxide, iodine, chlorine, bromine, salts of mercury, copper, and of silver. Hence, one must distill for some time before forming an opinion that no luminescence is going to appear. On account of this interference of such substances as those named with the luminosity of phosphorus, one must examine the distillate for free phosphorus or, at least, oxidize the filtrate and then test it for the presence of phosphates. If any considerable amount of phosphorus is present in the material submitted to distillation, minute globules of phosphorus may be noted at the bottom of the receiving flask. If such globules are present, they may be removed, washed with alcohol and finally dissolved in carbon disulphide. If, now, the solvent be allowed to evaporate in the dark, the characteristic luminosity will appear, especially if the residue be lightly rubbed.

If no globules are seen in the receiving flask, evaporate a considerable portion of the distillate on the water-bath, adding an excess of chlorine water, bromine water, or strong nitric acid. Take up the residue with a little water and test the solution both with ammonium molybdate in nitric acid solution and with magnesia mixture for the presence of the phosphoric acid ion. While a positive result in these tests is strong evidence of the presence of phosphorus in the material subjected to distillation, yet it is possible that small particles of phosphoric acid may have been carried over into the distillate or that hypophosphites or phosphites used for therapeutic purposes may have been present and may have been carried over and later oxidized to phosphoric acid, although such possibilities rarely need to be considered. However, we must still regard the presence of phosphorus sesquisulphide, as accountable for the phosphate reaction. In some cases this compound may be recognized by the yellowish deposit in either the condenser or in the receiving flask and by the peculiar mercaptan-like odor in the distillate, but at times such signs are confusing as these may come from decomposition of protein material. As a matter of fact the only reliable means of determining whether phosphorus sulphide or elementary phosphorus is present is the test of Schenck and Scharff, which will be outlined later.

In the process of distillation by the Mitscherlich method, a considerable amount of the phosphorus undergoes oxidation in the distilling flask and does not, of course, pass over into the distillate. For this reason the yield of phosphorus by this method is far from quantitative, Autenrieth[1] finding only 71.33 per cent. of phosphorus in the distillate. In order to prevent such oxidation and the consequent conversion of the phosphorus in the distilling flask to phosphoric acid, phosphorous acid, hypophosphorus acid and red phosphorus, Scherer[2] recommended distilling in a current of carbon dioxide. This modification prevents the appearance of the characteristic luminosity, even in the absence of such interfering substances as previously mentioned, but by the improvement suggested by Nattermann and Hilger[3] the phosphorescence may be made to appear and disappear at will. If the phosphorus vapor be conducted into a solution of silver nitrate, as in the methods of Fresenius and Neubauer[4] or of Nattermann and Hilger, black silver phosphide will be formed along with metallic silver and phosphoric acid, owing to the oxidation by the nitric acid liberated in the reaction. This black precipitate should not, without further examination, be regarded as proving the presence of phosphorus, as such substances as hydrogen sulphide, arsine, stibine, formic acid or formaldehyde (the latter being usually present in embalmed bodies) will, also, give a black precipitate, which will, however, not respond to the later tests for phosphorus. Instead of using these methods, the distillate obtained in the Mitscherlich test may be treated with silver nitrate solution, the black precipitate being filtered off, washed in water, and then used in the following test.

Dusart-Blondlot Test.—This test[5] responds to elementary phosphorus, hypophosphorous and phosphorous acids, phosphorus sesquisulphide, but not to phosphoric acid. It is based on the fact that hydrogen containing vapor of phosphorus or hydrogen phosphide, when ignited, burn with a characteristic green flame. The process consists of two steps: (1) the formation of a black precipitate of silver phosphide; and (2) the examination of this precipitate for phosphorus.

In the first step the elementary phosphorus or its lower oxidation products are reduced to phosphine (phosphuretted hydrogen, PH_3) by nascent hydrogen and this product is then passed into a neutral 3 per cent. aqueous solution of silver nitrate, when silver phosphide is formed, along with some free silver and phosphoric acid, owing to the oxidation of the phosphide by the nitric acid liberated in the reaction. As mentioned previously, this black precipitate cannot be considered as absolute evidence of the presence of phosphorus, as many substances, other than phosphine, will give a black precipitate.

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[1] *Detection of Poisons,* 6th Amer. Ed., 1928, p. 7.

[2] *Loc. cit.*

[3] *Forschungsber. über Lebensmit. u. ihre Beziehungen zur Hygiene,* 1897, **4,** 241. See, also, Fresenius, *Qualitative Chemical Analysis,* 17th Amer. Ed., 1921, p. 775 and Autenrieth, *Loc. cit.,* p. 18.

[4] Ztschr. f. anal. Chem., 1862, **1,** 340.

[5] See Dusart, Compt. rend. Acad de Science, 1856, **43,** 1126 and Blondlot, Ibid., 1861, **52,** 1197.

The finely divided material or the residue remaining in the distillation flask used in the Mitscherlich test (since phosphorus originally present in the material is partly oxidized and remains behind in this process) should be placed in a large flask containing pure phosphorus-free zinc (previously tested for phosphorus by this method) and water is added. Stopper the flask with a two-holed cork, through one hole of which passes a dropping funnel, while through the other passes a right-angle exit tube, the latter being connected with a large U-tube containing pieces of pumice stone saturated with concentrated sodium hydroxide solution to absorb any hydrogen sulphide that may be present in the tissues. The other end of the U-tube is attached to some form of absorbent apparatus containing 3 per cent. neutral silver nitrate solution. When the apparatus is ready, place dilute sulphuric acid (1:5) in the dropping funnel and allow enough of the acid to run in to maintain an active evolution of hydrogen, more acid being added as the evolution becomes slower, and continue the evolution of the hydrogen for some hours. As phosphine is a poisonous gas, great care must be taken to see to it that all connections are tight to prevent leakage of the gas being evolved. If a black precipitate forms in the silver nitrate solution, this indicates the possible presence of phosphorus or its lower oxidation products, but cannot, in itself, be considered conclusive. This precipitate is collected on a small ash-free filter paper, is washed with cold water and examined for phosphorus as directed below. The filtrate from this precipitate is treated with dilute hydrochloric acid to precipitate the silver, is filtered through a filter paper well washed with dilute nitric acid and water, and the free hydrochloric acid expelled by repeated evaporation with nitric acid on the water-bath. Dissolve the precipitate in a little water and test for phosphoric acid by both ammonium molybdate and magnesia mixture in the usual manner.

The examination of the silver precipitate should be made as soon as possible after the precipitation is complete. Set up the following apparatus. A small flask of about 100 cc. capacity with a wide neck is fitted with a cork having three holes, two of which bear tubes bent at right angles which terminate just below the cork, while the third bears a thistle tube reaching to the bottom of the flask (Fig. 39). A Kipp generator is attached to a wash-bottle containing water and then to the small flask, which latter is then attached to a U-tube containing pumice stone saturated with concentrated sodium hydroxide solution. To the U-tube is attached a tube of hard glass into the outer end of which is fused a platinum tip. Place in the small flask some phosphorus-free zinc and add the filter paper containing the silver precipitate (which paper should be cut into small pieces), adding sufficient water to seal the end of the thistle tube. Conduct pure hydrogen from the Kipp generator through the apparatus, and after it has passed for some time to expel all air, ignite the gas and observe whether the flame is colorless, taking all precautions, of course, to prevent explosions. When the purity of the hydrogen has been proven, allow a few cc. of dilute (1:5) sulphuric acid to flow into the thistle tube and again note the color of the flame. In the presence of phosphorus, the flame will burn with a green cone or a greenish glow. If a long narrow tube be held over the flame in such a manner that the flame is depressed against the inner wall of the tube, a green luminescence will appear through the whole tube, while phosphorescent light waves may appear.[1] The method is extremely delicate, Nattermann and Hilger[2] being able to detect 0.06 mg. of phosphorus in the form of phosphite with the naked eye, although the method can not be used for quantitative purposes, as only about 1/10 to, at most, 1/5 of the phosphite ion could be obtained as silver phosphide. To make the test more certain, the greenish flame should be examined with the spectroscope, even the smallest trace of phosphorus being characterized by two pale-green lines between which lies a faint green line, all lying to the right of the D line. It should be remembered that it is not always possible to obtain zinc which is absolutely phosphorus-free, so that possible errors may be introduced from this factor, while volatile phosphorus-containing substances may be formed in putrefying tissues, especially in brain tissue, and these may give the Dusart-Blondlot test. Hence this test is, often, not as conclusive as is the phosphorescence in the Mitscherlich test, especially when the latter is performed by the Nattermann and Hilger modification.

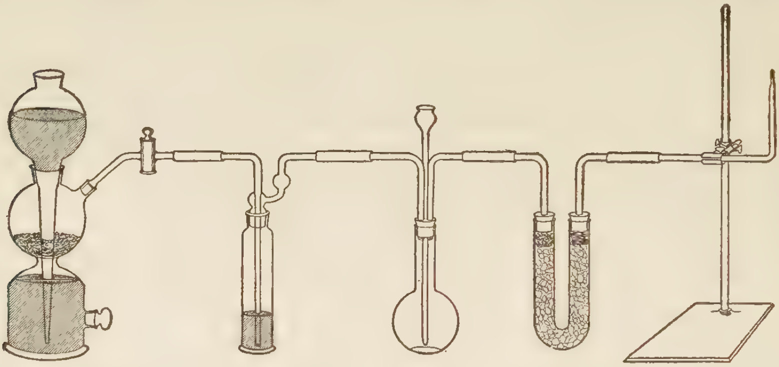

Fig. 39.—Hilger—Nattermann apparatus. (From Autenrieth and Warren "Detection of Poisons," P. Blakiston's Son & Co., Publishers.)

Schenck and Scharff Test.—This method of detecting phosphorus in the presence of phosphorus sesquisulphide is based on the fact that the vapor of the former, even in small quantities, ionizes the air so that it becomes a conductor of electricity, while those of the latter do not. In consequence, phosphorus vapor will discharge a charged electroscope, while phosphorus sesquisulphide has no action on the electroscope, especially at temperatures up to 50° and no appreciable action even up to 75°. A current of air is passed over the substance under investigation, which is heated to 50°C. and is then conducted into a completely closed cylindrical metal dissociation chamber, upon the cover of which is placed an insulated electroscope, from which a dissociating body extends downwards into the cylinder. If the charged electroscope shows a decrease in tension as evidence of discharge of the electroscope, white phosphorus is present, while, if no change is observed phosphorus sesquisulphide may be present, provided the Mitscherlich and Dusart-Blondlot tests have proven positive. The details of the method should be learned from the original article.[1]

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[1] See Dalmon, Ztschr. f. anal. Chem., 1871, **10**, 132.

[2] *Loc. cit.*

Determination.—The quantitative determination of the phosphorus in a case of suspected poisoning is not absolutely accurate, as the yield is slightly less than the known quantity present in experimental work. However, if estimations are to be made either the Fresenius-Neubauer or the Nattermann-Hilger methods of liberation of the phosphorus in an atmosphere of carbon dioxide to prevent oxidation of phosphorus to the products previously mentioned should be employed, the liberated phosphorus vapor being conducted into silver nitrate solution to form silver phosphide. After the process has been conducted for some hours, the contents of the receiving flasks, containing the silver phosphide together with the metallic silver and phosphoric acid, are evaporated upon the water-bath with an excess of aqua regia, the residue extracted with hot water containing a few drops of dilute nitric acid and filtered. Evaporate the filtrate to a small volume, add ammonia to strong alkaline reaction and precipitate the phosphoric acid by addition of magnesia mixture in the usual manner. Filter, wash the precipitate with water containing dilute ammonia, dry and ignite in the usual manner, weighing the precipitate as magnesium pyrophosphate. If the amount of $Mg_2P_2O_7$ be multiplied by 0.2785 the quantity of P, as such, in the amount of tissue taken for the test will be obtained. The yield by this method varies from 92 to 95 per cent. of the phosphorus present.

BORON

This element does not occur in nature in the free state, but is found in several parts of the world in the form of boric acid and its salts, tincal or native borax, boracite, and borocalcite. It is present in sea water in appreciable amounts and appears to be constantly present in all animal tissues as well as in most vegetables and fruits.[2] In fact, it has been shown to be almost indispensable to the proper growth of the higher types of green plants[1], although Conner[2] contends that a very small amount is poisonous to plants. Boric acid and its salts have been widely used by the medical profession as a bactericidal agent and such use has extended to the household, while this germicidal action on organisms that cause fermentation and putrefaction of solid and liquid foods has led to its rather wide usage in the preservation of food products, although it is doubtful whether it has any action on organisms of the colon group. On the basis of experimental evidence, although it must be said that there is much evidence on both sides of the question, it has been generally recognized that there is a potential danger in the use of boric acid and borax as preservatives of food, so that its use for this purpose has, for some time, been forbidden in the United States, Germany, Holland, Italy and Spain, while in Great Britain its use has only recently been prohibited.

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[1] Ber. d. d. chem. Ges., 1906, **39,** 1522. See, also, Autenrieth, *Detection of Poisons,* 6th Amer. Ed., 1928, p. 476.

[2] See Kobert, *Lehrbuch der Intoxikationen,* 2te Aufl., 1906, **2,** 61; also, Bertrand, Jour. Amer. Med. Assoc., 1914, **62,** 549; and Moscati, Arch. d. sci. biol., 1922, **3,** 279.

While the common use of boric acid and borax have led to the impression that it is relatively harmless, yet the literature reveals at least 16 cases of boric acid poisoning and 3 of borax poisoning,[3] all of them accidental and six of them occurring in hospital practice where a saturated solution was given, in mistake for distilled water, to infants of very tender years.

Boric Acid (H_3BO_3).—This acid, also called boracic acid, when dried to constant weight contains not less than 99.5 per cent. of H_3BO_3. It occurs in the form of transparent, colorless scales of a somewhat pearly luster, or hexagonal triclinic crystals, or a white bulky powder, slightly unctuous to the touch. It is stable in the air, has a slightly bitter taste, and shows a slight acid reaction when in aqueous solution. One gram of boric acid is soluble in 18 cc. of water, 18 cc. of alcohol, and in 4 cc. of glycerin at 25°C., while one gram is soluble in 4 cc. of boiling water and 6 cc. of boiling alcohol.

Borax ($Na_2B_4O_7.10H_2O$).—This salt, known, also, as sodium borate, sodium tetraborate, or sodium pyroborate, is a derivative of tetraboric or pyroboric acid, which is formed by heating boric acid to about 160°C. and contains not less than 52.32 per cent. and not more than 54.92 per cent. of the anhydrous $Na_2B_4O_7$, which corresponds to not less than 99 per cent. of the crystallized salt. It occurs as colorless, odorless, transparent, monoclinic prisms, or as a white powder, which is efflorescent in warm, dry air. It has a sweetish taste and its aqueous solution is alkaline to litmus paper. One gram of this salt is soluble in 15 cc. of water and in about 1 cc. of glycerin at 25°C., and in 0.6 cc. of boiling water, while it is insoluble in alcohol.

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[1] See Sommer and Lipman, Plant Physiology, 1926, **1**, 231; also, Johnston and Dore, Science, 1928, **67**, 325.

[2] Circ. 84, U. S. Dep't. Agriculture, 1920.

[3] See Witthaus, *Medical Jurisprudence, Forensic Medicine and Toxicology*, 2nd ed. 1911, **4**, 311; McNally and Rust, Jour. Amer. Med. Assoc., 1928, **90**, 382; Birch, Brit. Med. Jour. 1928, **1**, 177.

Symptoms.—These consist of loss of appetite, epigastric pain and cramps, retching and, in some cases, almost persistent vomiting, diarrhea, emaciation, weak pulse, cold clammy skin, occasionally cyanosis, depression and collapse. In come cases an intense erythematous rash is observed, which may cover the whole body if the substance has been taken internally, or may be more or less limited to the seat of application if locally applied. Any or all of these symptoms, which occasionally result in death, may be observed after internal ingestion, after enemata, following the washing out of infected cavities with solutions, or from the packing of wounds with the powder. Both boric acid and borax are eliminated through the saliva, gastro-intestinal tract, the milk and the urine. As a result of its elimination through the kidney, signs of nephritis may be observed. Kahlenberg and Barwasser[1] state that boric acid may be detected in the urine 51 seconds after immersing the feet in warm saturated solutions. Although as Jay[2] has shown, a large amount of the boric acid is eliminated by way of the urine in from 11 to 18 hours, yet this acid and its salts are deposited in the tissues and may be detected therein. Although Bazin[3] was unable to detect borates in the intestinal contents or in the blood in his case of death following repeated enemas of boric acid in water, McNally and Rust[4] were able to report for the first time in the literature the distribution of boric acid in the bodies of six infants accidentally poisoned by being given a saturated solution of boric acid in mistake for distilled water. These authors showed that the brain and liver accumulate about the same and the higher percentages, the bowel an intermediate amount, while the heart, lungs, stomach, kidneys and diaphragm contained the lower percentages.

Fatal Dose.—In the cases of McNally and Rust from 3 to 6 grams proved fatal to six infants, while 15 grams of boric acid was fatal to an adult[5] and Birch reports the death of an infant who had consumed 1½ drams (5.6 cc.) of sodium borate and boric acid in the form of honey of sodium borate and glycerin of borax,[6] while Potter[7] describes a case of fatal borax poisoning in an adult from the taking of something over an ounce of borax in mistake for a saline laxative.

Fatal Period.—Death has occurred in 3½ hours but usually does not happen for a few days after intake of these substances.

Treatment.—Prompt removal of the poison remaining in the stomach and bowels should be attempted by means of gastric lavage and enemata, while, if the poison has been locally applied, this should be washed off the wound or the cavity which was irrigated should be washed out with water. General eliminatory and symptomatic treatment should follow these initial steps.

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[1] Jour. Biol. Chem., 1928, **79**, 405. See, also, Kahlenberg, Ibid., 1924–25, **62**, 149.

[2] Ann. d'Hyg., 1897, **37**, 493.

[3] Canad. Med. Assoc. Jour., 1924, **14**, 419.

[4] *Loc. cit.*

[5] Schwyser, New Yorker med. Monatschr., 1895, **8**, 264.

[6] Brit. Med. Jour., 1928, **1**, 177.

[7] Jour. Amer. Med. Assoc., 1921, **76**, 378.

Postmortem Appearances.—The autopsy findings may be almost negative or there may be slight irritation of the gastro-intestinal tract, together with evidences of acute degenerative processes in the liver and kidneys.

Detection.—Although it matters little whether the material be taken in as boric acid or as borax, as the symptoms are practically the same, it is advisable to learn, if possible, in what form the substance exists. This may be done by extracting the finely divided tissue with warm water and testing the reaction of the extract. A strong alkaline reaction would indicate the probable presence of borax unless the tissues were strongly decomposed, while an acid, neutral or very faintly alkaline reaction would speak for the presence of free boric acid. Such tests are by no means absolutely reliable, but are presumptive.

Dry some of the suspected tissue at as low a temperature as possible, add a mixture of sodium carbonate and sodium nitrate and fuse the mixture until well ashed. Take up this residue with a little water and test as follows for the presence of borates.

1. Place a small amount of the aqueous extract in a porcelain dish, acidify with sulphuric acid and add some alcohol, stirring the mixture thoroughly. If the alcohol be ignited, the flame is colored green, especially at the edges, if boric acid is present. If this flame be examined with the spectroscope, it will show 4 lines in the yellow, green and blue.

2. Acidify another portion of the aqueous extract with hydrochloric acid and saturate a piece of turmeric paper with this solution, allowing the paper to dry at a low temperature. In the presence of boric acid this paper is colored a reddish-brown, which color is changed to a dark greenish-blue by caustic potash.

Determination.—The method used for quantitative estimation of the boric acid is as follows.[1] Make 100 grams of the finely hashed tissue distinctly alkaline with sodium hydroxide solution and evaporate to dryness in a platinum dish. Ignite the residue until the organic matter is thoroughly charred, avoiding an intense red heat; cool, digest with about 20 cc. of hot water and add strong hydrochloric acid, drop by drop, until the reaction is distinctly acid. Filter into a 100 cc. volumetric flask and wash with a little hot water, so that the volume of the filtrate does not exceed 50 cc. Return the filter containing any unburned carbon to the platinum dish, make alkaline by wetting thoroughly with lime water, dry on a steam bath, and ignite to a white ash. Dissolve the ash in a few cc. of dilute hydrochloric acid (1:3) and add to the liquid in the 100 cc. flask, rinsing the dish with a few cc. of water. To the combined solutions, add 0.5 gram of calcium chloride and a few drops of phenolphthalein indicator, then 10 per cent. sodium hydroxide solution until a permanent light pink color is produced, and finally dilute to the mark with lime water. Mix, and filter through a dry filter. To 50 cc. of the filtrate add N sulphuric acid until the pink color disappears, then add methyl orange indicator, and continue the addition of the acid until the yellow color is changed to pink. Boil for about 1 minute to expel carbon dioxide. Cool, and carefully add 0.2 N sodium hydroxide until the liquid assumes a yellow tinge, avoiding an excess of the alkali. All the boric acid is now in the free state with no uncombined sulphuric acid present. Add about 10 grams of neutral mannitol (or a volume of neutral glycerin equal to the volume of the solution to be titrated) and a few drops of phenolphthalein indicator; note the burette reading; and again titrate the solution with the standard sodium hydroxide until a pink color develops. Add a little mannitol or glycerin and, if the pink color disappears, continue the addition of the standard alkali until a pink color again appears, repeating the alternate addition of mannitol or glycerin and standard alkali until a permanent end point is reached. One cc. of 0.2 N sodium hydroxide solution is equivalent to 0.124 gram of boric acid. Hence multiply this figure by the number of cc. of standard alkali used and this result by 2 to obtain the amount of boric acid in the 100 grams of tissue originally taken.

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[1] *Official and Tentative Methods of Analysis of the Association of Official Agricultural Chemists,* 2nd ed., 1925, p. 131. See, also, *Volumetric Analysis* by Sutton, 11th ed., 1924, p. 97.

CHAPTER XIX

METALLIC POISONS

POTASSIUM

It must be recalled that the potassium ion has a distinctly poisonous action, which is chiefly manifested in depression of the central nervous system and of the heart. In mammals the chief nervous symptoms are great muscular weakness and apathy, the respiration becomes rapid and labored and death may be preceded by weak asphyxial convulsions. When introduced parenterally the potassium ion has a marked, almost specific action on the heart and circulation. Depending on the dosage, this action may be manifested by a fall in blood pressure; by dilatation and diminished cardiac output; immediate stoppage of heart in diastole; marked sinus slowing; partial or complete heart block; ventricular fibrillation with feeble auricular contractions; and final arrest of heart beat. However, administration of potassium salts by mouth does not ordinarily exercise such marked effects upon the circulation, the chief effects being a slower and weaker pulse and often a sudden fall in blood pressure. Absorption from the alimentary tract does not keep pace with the elimination from the kidney, so that the potassium is not accumulated in the blood in sufficient amounts to cause the marked toxic symptoms. Further, it is possible that potassium salts have an irritating action on the gastric mucosa.

The above actions of the potassium ion are common to practically all salts of potassium, in contradistinction to the almost inert property of the sodium and ammonium ions, with which the potassium ion is closely related chemically. In toxicology, however, we rarely, if ever, have occasion to consider this toxic action of the potassium ion, as such symptoms are not ordinarily shown when salts of potassium are taken by mouth. It is, therefore, to the anion with which the kation, potassium, is bound, that we must look for the toxicological action with which we are especially concerned here. Possibly, these salts might be discussed under the heading of the acids from which they are derived, but for convenience it seems advisable to take them up in this connection.

Potassium Chlorate

This salt, $KClO_3$, is widely used in the manufacture of explosives and in match heads, and finds rather frequent application in medicine. It is a somewhat common household remedy, being employed as a mouth wash or gargle in cases of sore mouth and throat. For this reason it has been looked upon as more or less harmless, but it has great potential power for harm and has frequently lead to cases of poisoning. Although it is, as Dreser[1] has shown, less toxic than either the iodate or bromate, yet we find that these latter halogen compounds are almost never used as poisons. Witthaus[2] collected from the literature 155 cases of poisoning from potassium chlorate, 116 of which were fatal; most of these were accidental; 15 were suicidal; and 3 were homicidal. While it is, of course, possible for sodium chlorate to produce the same toxic effects as the potassium chlorate, yet we find, according to Witthaus, only one case of poisoning from the former salt, due, probably, to the fact that it is rarely used either in medicine or the arts.

Properties.—This salt occurs as colorless, odorless, lustrous, monoclinic prisms or plates, or a white granular powder, which is stable in the air. It is readily soluble in water and in glycerin, but almost insoluble in alcohol. It must be handled with care, as explosions may occur when it is heated or subjected to concussion or to trituration with such organic substances as cork, tannic acid, sucrose, etc., or with charcoal, sulphur, sulphides, hypophosphites, or other easily oxidizable substances.[3]

Symptoms.—The action of potassium chlorate is both local and general. In the rapidly progressing cases there is severe vomiting, profuse diarrhea, marked epigastric and abdominal pain, intense dyspnea, deep cyanosis, greatly lowered blood pressure and cardiac weakness. The most marked general action is exerted upon the red blood corpuscles, the hemoglobin being converted into methemglobin with the production of a chocolate-colored blood. The blood corpuscles at first appear normal in shape, but the hemoglobin is more brownish in color, later the corpuscles appear shrunken and the hemoglobin passes out of the cell to a large extent. This leads to such secondary symptoms as jaundice, methemoglobinuria, and signs of marked irritation of the kidneys. The cardiac effects are, at least in part, due to the action of the potassium ion. According to Kobert the conversion of the oxyhemoglobin to methemoglobin may be so marked that the oxygen content of the blood may sink to as low as 1 per cent. The changes in the organs are usually in proportion to the extent of the methemoglobinemia, the kidney, perhaps, showing the most intense effects. Sooner or later uremia supervenes and the patient dies in coma. In some cases the disintegration of red cells may be so great that fatal embolism may arise.

In the less severe cases all of the above symptoms may be observed only in a less intense degree. Probably the kidney changes are better noted in these cases, which are not so rapidly fatal. So, also, the characteristic changes in the blood corpuscles are better studied in the cases of slower progression. The number of red cells is diminished, irregular forms are noted, especially prominent being the shadow cells, the ovoid types, the crenated forms, and the tendency of the cells to agglutinate.

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[1] Arch. f. exp. Path., 1894, **34,** 207.

[2] *Medical Jurisprudence, Forensic Medicine and Toxicology,* 1911, **4,** 690.

[3] See *Pharmacopoeia of the United States,* 10th Dec. Rev. 1926, p. 299.

The number of white cells may be increased and the degree of alkalinity of the blood is lowered. Unchanged potassium chlorate may be found in the urine in a relatively short time after its ingestion and sooner or later all the urinary evidences of an acute nephritis will be forthcoming, along with the appearance of hemoglobin and methemoglobin in the urine. The liver and spleen are usually enlarged and the patient complains of pain and tenderness in the region of the liver. Nervous symptoms may be prominent, delirium, coma, violent tonic or clonic convulsions, and fixation of the muscles of the extremities being often noted.

Fatal Dose.—Apparently this poison shows a peculiar action in that a certain amount, given in divided doses over a period of a few days, may show a more severe reaction than if the same amount were taken in one dose. Thus the smallest single dose, according to Witthaus, that has caused death was 14 grams taken by an adult who died in 4 days,[1] while 11.75 grams taken by an adult over a period of 3 days was fatal.[2] The minimum lethal dose, actually known to have caused death of an adult, is the case cited above, while a doubtful case of death from the exceedingly small dose of 6 grains (0.4 gram) is reported[3]. Death of a child of less than 1 year of age has occurred from 3.9 grams[4], while an infant[5] of 3 weeks died from the effects of 1 gram. On the other hand, very much larger doses have been taken without causing death. Thus 46.7 grams (719 grains) have been taken by an adult during a period of 13 hours and recovery followed,[6] while Hofmann[7] states that 23 grams have been taken by an adult within 12 hours without causing symptoms of poisoning.

Fatal Period.—Witthaus states that "the average duration of 90 fatal cases in which it is stated was 4 days and 9 hours." Death in 1 hour[8] has been reported, but this case is a very doubtful one. While death may occur in a few hours, many of the cases do not die for several days.

Treatment.—Potassium chlorate is quite rapidly absorbed from the gastrointestinal tract, but, nevertheless, the stomach should be promptly washed out to remove any poison remaining. Diuresis should be promoted by administration of alkaline drinks, and elimination through the saliva may be stimulated by hypodermic administration of pilocarpine. The cardiac and respiratory depression will require appropriate stimulants. In some cases inhalation of oxygen may prove of value.

Postmortem Appearances.—Evidence of gastro-intestinal irritation will usually be found. However, the most characteristic findings are due to the change of the oxyhemoglobin to methemoglobin. This change in the blood gives to the whole body a peculiar gray appearance. According to the intensity of the blood changes, the blood may appear of a grayish-brown, a chocolate brown, or a darker brown resembling in color tobacco juice or coffee grounds. The blood in proper dilution may show the characteristic spectrum of methemoglobin. These changes may not be present if death occurred some time after the poisoning or if the autopsy was performed a few days after death. The liver, spleen and kidneys are usually enlarged and are filled with decomposition products of hemoglobin. The kidney shows especially characteristic changes, the tubules being filled with brownish masses of blood detritus, which gives a peculiar chocolate colored striped appearance to the pyramids. The brain may appear as if injected with chocolate, the vessels as though filled with chocolate colored blood.

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[1] Riess, Arch. f. exp. Path. und Pharm., 1908 Supplb., 461.

[2] Zillner, Wien. med. Wchnschr., 1882, **32**, 1331.

[3] See Vienna letter, Jour. Amer. Med. Assoc., 1907, **49**, 1930.

[4] Hall, Med. Rec., 1878, **14**, 396.

[5] Goldschmidt, Breslau. aerztl. Ztschr., 1883, **5**, 6.

[6] Gesenius, Deutsch. med. Wchnschr., 1882, **8**, 512.

[7] "Lehrbuch der gerichtlichen Medizin," 11te. Aufl., 1927, p. 861.

[8] See Vienna letter, Jour. Amer. Med. Assoc., 1907, **49**, 1930.

Detection.—Concerning the detection of potassium chlorate in the organs of the body, it is to be said that the chance of finding it is relatively slight, if the body has been buried some time or if decomposition is at all advanced, owing to the rapid reduction of the chlorate to chloride. Further, the methemoglobin may be converted back to hemoglobin in the process of putrefaction, so that this sign may also fail. However, it may occasionally be detected in the urine, stomach and intestinal contents, liver and kidneys, but the amounts found will usually be small, as this salt is rapidly eliminated and, also, quite rapidly converted into chloride in the body.[1]

The salt may be extracted from the finely divided tissue by means of warm water or, preferably, by submitting a watery mixture of the tissue to dialysis against a small amount of distilled water, all diffusible elements, of course, being found in the dialysate. This dialysate may then be concentrated, if necessary, at a low temperature and the qualitative tests performed.

1. If a little of the dialysate be colored light blue with a small quantity of a solution of indigo in sulphuric acid, a little dilute sulphuric acid added, and then, drop by drop, a small quantity of aqueous sulphur dioxide or solution of sodium sulphite, the color of the indigo will immediately disappear in the presence of a chlorate in the dialysate.

2. If a little of the dialysate be treated with a little starch paste and a solution of potassium iodide and strong hydrochloric acid be added, on warming the mixture a blue color will appear, owing to the liberation of iodine from the iodide by the chlorine set free from the chlorate and the later formation of blue iodide of starch.

Determination.—Take a weighed portion of the finely divided tissue or a measured portion of the contents of the stomach or of the urine, add some distilled water to the tissue and dialyze in a cool place against distilled water over night, adding a little toluol to the mixture in the dialyzer to prevent decomposition. Make the dialysate up to a standard volume and determine the amount of the chlorine ion present as chloride in $\frac{1}{2}$ of this solution, by titration with standard silver nitrate in nitric acid solution in the usual manner. The remaining half of the original dialysate is then evaporated to dryness with the addition of chlorine-free sodium carbonate and the residue heated to redness in order to reduce any chlorate present to chloride. Now determine the amount of the chlorine ion present in the watery extract of this residue and subtract the former value from the latter, which will represent the chlorine originally present in the form of chlorate. If the chlorine value, obtained by this subtraction, be multiplied by 3.456 the result will be the amount of potassium chlorate present in ½ of the amount of original material taken. Hence, multiply this figure by 2 to obtain the amount of chlorate in the original tissue taken.

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[1] See Lacassagne, Arch. d'anthrop. crim., 1887, **2**, 359.

Potassium Nitrate

Potassium nitrate, also known as nitre and saltpeter, is widely used in the manufacture of gunpowder and of fireworks and has found occasional use in the pickling of meats and cucumbers, and, also, as a therapeutic agent. The sodium nitrate is extensively employed as a fertilizer. Quite a few cases of poisoning from the potassium salt have occurred, while few, if any, have been reported as due to the sodium salt. Witthaus has collated the reports of 33 cases of potassium nitrate poisoning, and refers to 6 others which were not accessible to him. Many of these cases have been due to the mistaking of the nitrate for such salts as magnesium sulphate, sodium phosphate, and, even, sodium chloride.

Potassium nitrate occurs as colorless, transparent, six-sided rhombic prisms or as a white, crystalline powder. It is odorless, has a saline taste and is slightly hygroscopic in moist air. It is readily soluble in water and glycerin, but not readily soluble in alcohol (1 part in 620).

Symptoms.—The symptoms following ingestion of large doses of potassium nitrate are due to the action of both the potassium and the nitrate ions. There is pain in the stomach and abdomen, vomiting, purging, which may often show bloody stools, localized muscular contractions, general weakness, labored respiration, weak cardiac action and collapse. The pulse is at first accelerated, but later becomes slow and weak. In some cases there may be delirium with much excitement, followed by coma and collapse.

Fatal Dose.—Death has occurred from 8 grams administered in an enema[1], while 30 grams has caused death when taken per os.[2] However, recovery has followed the taking of much larger doses.

Fatal Period.—Probably the most rapidly fatal case is the one of Chevalier, de Luynes and Devergie[3] of death in 45 minutes, while the longest survival was 17 days after the patient came under treatment following the daily intake of 10 grams of potassium nitrate for 26 days.[4]

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[1] Meyer, St. Petersb. verm. Abh. d. Heilkde., 1823, **2**, 88.

[2] See Taylor, "On Poisons" 3rd Amer. Ed., 1875, p. 263.

[3] Ann. d'Hyg., 1861, 2 S., **17**, 400.

[4] Windmueller, Jour. Amer. Med. Assoc., 1921, **77**, 858.

According to Witthaus, the average of eleven fatal cases, in which the duration was stated, was 13 hours.

Treatment.—There is no specific antidote. Vomiting should be promoted by the use of emetics and, later, gastric lavage should be practiced. Mucilaginous drinks may be given to soothe the irritated gastric mucosa. Symptoms of collapse should be treated as they arise.

Postmortem Appearances.—The autopsy findings in the reported cases seem to indicate that the principal lesions are found in the stomach in the form of a hemorrhagic gastritis, in one case a small perforation being found at the fundus.

Detection.—Potassium nitrate is rapidly absorbed from the stomach and rather quickly excreted by the urine. However, it has been detected in the gastric contents, liver, kidneys and other organs in several cases. Probably the best procedure to follow is to subject the finely divided tissue or the urine, stomach contents, etc., to dialysis against a small amount of distilled water. Concentration of the dialysate should then be carried out. If sulphuric acid be added to the residue, nitric acid is set free and may be detected by the tests outlined previously under this acid.

Determination.—While quantitative estimations of the amount of nitrate present are usually of little value, inasmuch as much of the nitrate ingested may have been lost through vomiting and purging, as well as by elimination through the urine, yet in some cases such determinations may be advisable. If this be desired, one may dialyze a weighed amount of the hashed tissue mixed with water against distilled water over night, adding toluol to prevent decomposition and reduction of the nitrate to nitrite. The nitrate present may then be determined by the quantitative method outlined under nitric acid.

POTASSIUM BITARTRATE

This salt, also known as *cream of tartar* and potassium acid tartrate, is frequently used in the household, is a constituent of some baking powders, and is not infrequently employed as a therapeutic agent. The potassium and sodium tartrate (*Rochelle salt*) and its official preparation, the Seidlitz powder (*pulvis effervescens compositus*) also find common therapeutic use. Although it has been regarded as more or less harmless, free tartaric acid has been reported as causing death in several cases.[1] Potassium bitartrate has proven fatal in at least 2 cases,[2] while dangerous symptoms have arisen from the taking of Seidlitz powders.[3]

Tartaric acid occurs as colorless, translucent crystals, or a white granular or fine powder. It is odorless, has an acid taste, and is stable in the air. It is easily soluble in water and alcohol, slightly soluble in ether and almost insoluble in chloroform. Potassium bitartrate occurs as colorless or slightly opaque, rhombic crystals, or as a white, somewhat gritty powder. It is odorless, has a pleasant, acidulous taste, and is stable in the air. It is soluble in 155 parts of water and in 8820 parts of alcohol. Potassium and sodium tartrate is found in the form of colorless, transparent, rhombic prisms, or a white powder, it is odorless, has a cooling, saline taste, and is slightly efflorescent in dry air. It is readily soluble in water, but practically insoluble in alcohol.

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[1] See Gill, Lancet, 1845, **1**, 18; Devergie, Ann. d'Hyg., 1851, **46**, 432 and 1852, **47**, 383; Orfila, Ibid., 1852, **47**, 199; Trevithick, Brit. Med. Jour., 1893, **1**, 1321; Connio, Pathologia, 1910, **3**, 428.

[2] See Tyson, Lancet, 1837–38, **1**,162; and Roger, Friedreich's Bl. f. ger. Med., 1887, **38**, 196.

[3] See Buel, Amer. Jour. Med. Sci., 1858, **36**, 570; Triplett, Med. News, 1893, **63**, 548; Gaithes, Jour. Amer. Med. Assoc., 1924, **83**, 195.

Symptoms.—These are usually referred to the gastro-intestinal tract. There is violent vomiting and purging, pain in the abdomen, thirst, feeble pulse, occasionally paralysis in some groups of muscles, collapse and death. In Connio's cases of tartaric acid poisoning the renal symptoms were marked. In view of the experimental work of Baer and Blum, Underhill, Wells and Goldschmidt, Pearce and Ringer, Karsner and Denis, and others in the production of nephritis in animals by the parenteral administration of tartrates, one might expect that evidences of nephritis would be clear in poisoning from the tartrates in man, although we have no direct reports of such except by Connio.

Fatal Dose.—Tartaric acid has proven fatal in a dose of 12 grams, as reported by Trevithick, while potassium bitartrate is less toxic, the fatal doses, as reported by Tyson and by Roger, being 125 grams and 200 grams respectively.

Fatal Period.—With tartaric acid death has been reported in 7 and in 9 days, while with potassium bitartrate the reported deaths occurred in 12 hours and in four days.

Treatment.—This should be the same as outlined previously for oxalic acid and the oxalates.

Postmortem Appearances.—The stomach and intestines show signs of more or less irritation. In Connio's cases of tartaric acid poisoning, the kidneys showed quite a severe nephritis, which finding has been confirmed in cases of tartrate poisoning in animals, the microscopic appearances being especially marked in the convoluted tubules.

BARIUM

Besides being widely used in the chemical laboratory as reagents, some of the salts of barium are frequently employed in the arts. Thus, the chloride is used in the dyeing industry, the nitrate and chlorate in the making of Cassel green and the so-called "green fire", the chromate as a yellow dye, and the carbonate and oxide in the manufacture of glass. Further, some of these salts find rather different applications, as, for instance, the carbonate, which is mixed with arsenic trioxide in the well-known "Rough on Rats", the sulphide, which is used as a depilatory, and the sulphate, which is extensively employed in the form of barium meals in fluoroscopic and X-ray work. All of these salts, with the exception of the sulphate, are easily soluble in water or in dilute acids, so that it is not surprising to find reports of poisoning from most of them. Although many of the reported cases of poisoning have been due to mistakes in compounding medical prescriptions or to impurities in the sulphate, yet the number of poisonings is relatively rare in comparison with the wide employment of the sulphate in X-ray work.

Witthaus[1] collates the reports of 30 cases with 20 deaths, of which cases 14 were by the chloride, 10 by the carbonate, 4 by the nitrate, and 2 by the acetate. Of this group 22 were accidental, 3 were suicidal, 1 was taken to produce abortion, and in 4 the motive was not stated. Witthaus, also, refers to 4 other cases, to which he was unable to get access, and failed to include a death from barium chloride reported by Schuchardt. McNally, in 1925, in a review of the literature since 1910, found additional reports of 12 deaths from barium carbonate, 6 deaths from barium chloride and four from barium sulphide poisoning, to which should be added the two cases reported by him, one of barium sulphide and one of barium carbonate poisoning[2] and two cases of barium carbonate poisoning overlooked by him.[3]

Symptoms.—Shortly after swallowing the barium salt there is salivation, nausea, vomiting, severe epigastric pain followed by persistent purging. The patient complains of feeling cold, the skin is usually pale and there may be catarrhal affections of the conjunctiva and of the nose. There may be severe cramps in different groups of muscles, about ½ of the cases showing convulsions, and in other cases paralysis of the muscles of the extremities and trunk may be observed, while general muscular weakness is common. The pulse, in some cases, is small, irregular and intermittent, while in others it shows a digitalis-like action in being slow and full. The blood pressure is usually increased and the patient complains of cardiac palpitation. Associated with this may be noted vertigo, ringing in the ears, disturbances of vision, and disturbances of speech. Collapse and death may come on suddenly, associated with general convulsions and failure of respiration.[4]

Fatal Dose.—The smallest reported fatal dose of barium chloride appears to be 3 grams[5], although Kobert and Schedel believe that 2 grams might cause death under certain conditions and Hofmann-Haberda[6], quoting Stern, state that the fatal dose varies between 1 and 10 grams. As regards the fatal dose of the carbonate, it is to be said that 10 to 12 grams have caused death[7] while adults have recovered from much larger doses. Barium sulphide has proven fatal in doses of 38 grams, while 15 grams of the nitrate and 30 grams of the acetate have caused death.

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[1] *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 1911, **4,** 682.

[2] McNally, Jour. Amer. Med. Assoc., 1925, **84,** 1805.

[3] Baumann, Ztschr. f. Nahr. u. Genussm., 1922, **43,** 383; and Dinslage and Bartschat, Ibid., 1924, **47,** 7.

[4] See Ets, "Some Lesser Known Actions of Barium," Proc. Inst. Med. of Chicago, 1927, **6,** 247.

[5] Schuchardt, cited by Maschka, *Handbuch der gerichtlichen Medizin,* 1882, **2,** 170.

[6] *Lehrbuch der gerichtlichen Medizin,* 11te. Aufl., 1927, p. 848.

[7] Wolff, Deut. Ztschr., f. d. ges. gerichtl. Med., 1922, S. 522.

Fatal Period.—Death has occurred in ten minutes after the ingestion of 40 grams of the sulphide in mistake for the sulphate,[1] while in other cases the fatal outcome has been delayed for one or more hours, the average of 13 cases in which the period is given being stated by Witthaus to be 11 hours, although some cases last for 2 or 3 days.

Treatment.—Probably the best chemical antidote is a soluble sulphate, such as magnesium or sodium sulphate, to precipitate the barium as the insoluble sulphate. This should be followed by gastric lavage with milk and water. Heat should be applied to the body and the cardiac depression treated by stimulants as the symptoms arise. The abdominal pain and the marked slowing of the pulse may require the administration of atropine.

Postmortem Appearances.—The mucosa of the stomach and intestines may show a high-grade hyperemia with numerous petechiae throughout. The heart, liver, kidneys and spleen may show parenchymatous degeneration.

Detection.—The question of the possible presence of "normal barium" in the tissues has been raised from time to time. In this connection McNally[2] examined the organs of eleven cases with negative histories of poisoning and failed to obtain chemical evidence of the presence of barium in the liver, kidneys, bowel, and brain, although positive spectroscopic tests were obtained in all the organs except the brain. It should be recalled that some of our common condiments, such as vinegar and common salt, not infrequently contain small amounts of barium salts so that it might be expected that traces of barium might occasionally be found in organs examined toxicologically.

Elimination of barium occurs principally through the feces, although some is excreted in the urine. However, much of the intake of barium is stored up in various organs probably in the form of the sulphate. Outside of the stomach and bowels, the liver, kidneys, spleen and heart will probably show the largest amounts of barium, although in some cases little or none may be found in either the stomach or bowels.

As we have seen previously (page 340) barium will be found in the systematic analysis for poisons in the insoluble residue left after treating the tissues with hydrochloric acid and potassium chlorate by the method of Fresenius and von Babo, as well as partly in the filtrate from this residue. For this reason it is advisable to test the insoluble residue from such treatment for barium or one may use more direct methods if barium be suspected.

Treat the insoluble residue obtained in the process of Fresenius and von Babo or, if preferred, some of the hashed tissue is ashed and the ash fused with sodium carbonate. The cooled fusion is extracted with dilute hydrochloric acid, the solution filtered and the following tests for barium performed.

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[1] Bensaude and Antoine, Bull. et mém. Soc. méd. des Hôp. de Paris, 1919, **43**, 369.

[2] *Loc. cit.*

1. Addition of a little dilute sulphuric acid to the acid solution produces a white precipitate, insoluble in nitric and hydrochloric acids.

2. Neutralize some of the original hydrochloric acid solution with ammonia and add a little neutral solution of potassium chromate, when a yellow precipitate of barium chromate will form. This precipitate is soluble in hydrochloric and nitric acids, but only slightly soluble in dilute acetic acid and sodium or potassium hydroxide solution.

3. The solution of the barium salt colors the flame green. If this green flame be examined spectroscopically, two especially characteristic lines in the green, which lie near the Fraunhofer lines E and b, while two less prominent lines may be observed.

Determination.—If the above qualitative tests have proven positive, the direct determination of the barium in the tissues may be made as follows. Weigh out a definite amount of the hashed tissue, usually an aliquot part, make alkaline with a little sodium hydroxide and ash in a porcelain or nickel crucible. Dissolve the completely ashed material in a little dilute (10 per cent.) hydrochloric acid, dilute with water and precipitate the barium by the addition of sulphuric acid. Allow the precipitate to settle out, filter and wash it free from sulphuric acid. Place the filter paper and precipitate in a platinum crucible and ignite until the filter paper is completely burned. Add to the residue in the crucible some sodium or potassium carbonate and heat to fusion. Cool the fusion, extract with a little hot water to remove the alkali sulphate formed and the excess alkali carbonate, filter and wash the residue with a little water. As the quantitative conversion of the sulphate into the carbonate is rarely accomplished with one fusion, repeat the process as before. Digest the final fusion with dilute hydrochloric acid, filter, wash with hot water and precipitate the barium as sulphate as usual. Wash, dry and weigh the precipitate. The amount of barium carbonate, sulphide, or other salt may be calculated from the barium sulphate found.

MAGNESIUM

Magnesium salts have not ordinarily been associated with toxic properties, yet the literature reveals the fact that fatal poisonings have occurred and that toxic symptoms occasionally arise from the daily use of some of these compounds. Probably magnesium sulphate (Epsom Salt) is the most widely used cathartic and, if given well diluted with water, ordinarily produces its therapeutic effects without any untoward results, owing to the fact that the increased peristalsis moves the drug onward so rapidly that practically no absorption occurs. If, however, this onward movement be prevented by obstruction or is delayed by sluggish peristalsis, more or less of the salt may be absorbed, both from concentrated and dilute solutions, so that toxic affects may arise. If the salt does not exert its usual purgative effects, irritation of the intestinal mucosa may occur and magnesium will be absorbed from this irritated area. Probably the most extensive study of the action of magnesium sulphate as a toxic agent in man has been made by Boos[1], who reports 2 cases of his own and collates 8 other cases of magnesium sulphate poisoning, 6 of which were fatal. In only 1 of these was there active purging, and in 5 there was no purging whatever, due, probably, to paralysis of the bowel. Magnesium sulphate has been used to control the convulsions of tetanus, as it had been shown that repeated intravenous doses paralyzed the skeletal muscles and the reflexes. The respiration, however, was frequently abolished, so that the margin of safety was too small to permit of its general use for this purpose. While Finar[2] and later Rissman[3] advocated the intraspinal injection of magnesium sulphate in the treatment of eclampsia, this method has not been generally adopted. In his experiments upon animals Stander[4] found that intramuscular or intravenous injection of doses of magnesium sulphate ranging from 0.05 to 0.49 gram per kilo of weight produced definite histologic changes in the liver and kidneys. For human beings Stander regards the nontoxic dose as not over 0.1 gram per kilo. Attempts to use the subcutaneous injections of solutions or magnesium sulphate as synergistic to morphine in the production of local and general anesthesia, according to the method of Gwathmey[5], have resulted fatally in some cases.[6] Occasionally, there may be sufficient arsenic as an impurity in magnesium sulphate to produce very severe and even fatal results.

Magnesium oxide and carbonate have been widely used in the treatment of gastric ulcer as ant-acids, along with sodium bicarbonate and calcium carbonate. In some cases untoward results have been noted, but no fatal accidents have, so far as we can find, been reported. The toxic symptoms noted, which seem to be produced by any of these alkalies in certain cases, are headache, anorexia, nausea and vomiting, lassitude, and, occasionally, signs of impaired renal function. It is clear, therefore, that patients with gastric ulcer, who show such a train of symptoms following administration of these ant-acids, and, especially, those who have associated renal disease, should not be forced to continue this method of controlling the hyperacidity of the gastric juice, as symptoms of alkalosis are, unquestionably, present.[7]

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[1] Jour. Amer. Med. Assoc., 1910, **55**, 2037. See, also, Prestley, New York Med. Jour., 1912, **96**, 665; Anderson, Jour. Med. Assoc. Georgia, 1921, **10**, 826; and Thatcher, Jour. Amer. Med. Assoc., 1928, **91**, 1185.

[2] Amer. Jour. Physiol., 1905, **16**, 366.

[3] Zentralbl. f. Gynäk., 1913, **37**, 196.

[4] Jour. Amer. Med. Assoc., 1929, **92**, 631.

[5] Jour. Amer. Med. Assoc., 1921, **76**, 222. See, in this connection, Beckman, Jour. Lab. and Clin. Med., 1924, **10**, 189; Jour. Amer. Med. Assoc., 1925, **85**, 332; Gwathmey and Hooper, Jour. Lab. and Clin. Med., 1925, **10**, 641; Gwathmey. Jour. Amer. Med. Assoc., 1928, **91**, 1774.

[6] See Curtis, Jour. Amer. Med. Assoc., 1921, **77**, 1492.

[7] See Shattuck, Rohdenburg, and Booher, Ibid., 1924, **82**, 200.

Symptoms.—The usual symptoms observed are marked gastric and intestinal pain, nausea, vomiting and purging, although this latter symptom is by no means always present. Later, contractions of various groups of muscles may occur and general convulsions with collapse and death follow. Paralysis of respiration is not infrequently observed.

Fatal Dose and Fatal Period.—It is difficult to state the minimum fatal dose of magnesium sulphate, as large doses have been taken without producing any untoward results. Two ounces have produced death in 40 minutes[1], while 4 ounces have proven fatal in 75 minutes[2]. In the case of Curtis[3], in which 310 cc. of a 4 per cent. solution of $MgSO_4$ (12.4 grams) were injected subcutaneously, death occurred in 60 hours.

Treatment.—Measures should be adopted to increase the elimination by means of the urine and the feces. Large volumes of physiological salt solution may be given either subcutaneously or intravenously and calomel may be given for the action on the bowel.[4] As the respiratory depression may be especially marked in magnesium sulphate poisoning, intravenous injection of 0.02 per cent. calcium chloride in normal saline may prove efficacious in controlling this respiratory depression, or artificial respiration may be instituted.

Postmortem Appearances.—While large doses of magnesium sulphate may produce more or less irritation of the gastro-intestinal tract, yet the changes observed have not been marked. In the case of Curtis, there were intense jaundice, extensive acute fatty changes in the liver, and multiple petechial hemorrhages of the pleura, pericardium and endocardium.

Detection.—In the cases of Boos the high specific gravity of the urine indicated the marked elimination by way of the kidneys. It should be remembered that magnesium is a normal constituent of all tissues of the body, so that its mere detection does not prove poisoning in itself. The tissues are ashed in the usual manner, the ash taken up with dilute hydrochloric acid and filtered. To the filtrate ammonia is added in sufficient quantity to make the mixture slightly alkaline and the mixture warmed. Filter off the ferric hydroxide and, possibly, traces of aluminum hydroxide. To the filtrate add a little ammonium oxalate solution and allow to stand for a time in order to allow the precipitate of calcium oxalate to settle out. Filter and to the filtrate add sodium phosphate solution in excess and a little more ammonia and allow the mixture to stand over night, when a white crystalline precipitate of magnesium-ammonium phosphate appears if magnesium be present. Of course small amounts of magnesium are always found in tissues, so that the only value in such determinations is the quantitative estimation.

The quantitative determination is made by the above procedure, using a weighed amount of the hashed tissue. The precipitate of the triple phosphate is filtered, washed with dilute ammonia solution and dried in the oven. The filter and precipitate are then placed in a platinum crucible and heated until the paper is completely incinerated, after which the residue is heated over a blast lamp for 10 to 15 minutes to convert the triple phosphate into magnesium pyrophosphate, in which form the magnesium is weighed. If the amount of pyrophosphate be multiplied by 1.107 the result will be the amount of crystallized magnesium sulphate ($MgSO_4.7H_2O$) in the tissue taken.

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[1] See Christison, *On Poisons*, 1845, p. 574.

[2] Sang, Lancet, 1891, **2**, 1037.

[3] *Loc. cit.*

[4] See Fraser, Lancet, 1909, **1**, 1174.

ALUMINUM

Aluminum is probably the most widespread of all the metals, being found, according to Kobert, in about 200 minerals. It has, also, been reported[1] as present in most vegetables, in many fruits, in milk, eggs, and in sea food and as probably present in the tissues of the human and animal bodies, at least in traces. Besides the aluminum that is derived from the usual vegetable and cereal foods of man, some compounds of aluminum are taken into the system almost daily in mineral waters and in those city waters, which have been treated with aluminum compounds for the purposes of purification. A further source of supply of aluminum is found in the form of residues from the so-called S.A.S. (sodium-aluminum sulphate) baking powders. A bitter controversy has arisen over the alleged harmfulness of these aluminum residues of the hydroxide and phosphate, some claiming that aluminum compounds are general protoplasmic poisons and, also, that such residues are deleterious to the gastric processes, although the report of the Referee Board showed that "aluminum compounds when added to foods in the form of baking powders, in small quantities, have not been found to contribute any poisonous or other deleterious effect which may render the said food injurious to health".[2] It has been assumed that there was a possibility of absorption of such residues, at least in part, and that the tissues would, therefore, contain traces of what might be called "normal" aluminum. Recently McCollum, Rask, and Becker[3] have concluded from their experimental work, in which the detection of aluminum was carried out entirely by spectrographic methods thus eliminating the possibility of contamination with aluminum compounds which arise in the usual chemical processes, that aluminum is not a constituent of either plant or animal matter and that aluminum compounds are not absorbed out of the stomach or intestinal tract when present in the diet. They further showed that aluminum compounds in the diet in concentrations as high as 600 parts per million of the element aluminum exert no noticeably deleterious action on growth, reproduction, or general well being as judged by external appearance and autopsy. As these writers state: "These conclusions can probably not be regarded as final until after additional and confirming data have been obtained on a larger variety of materials and other animals." In checking the above work, Kahlenberg and Closs[1], using the same methods as the previous workers, arrived at quite different conclusions, finding aluminum to be present in egg, potato, carrot, English walnut meat, peach pit, apricot pit, pop-corn, lima beans, navy beans, lupine beans, peanut kernel, lean beef, beef tendon, and human cancerous tissue.

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[1] See Langworthy and Austen, *The Occurrence of Aluminum in Vegetable Products, Animal Products and Natural Waters,* 1904; Myers and Voegtlin," Soluble aluminum compounds, their occurrence in certain vegetable products", U. S. Weekly Public Health Reports, 1914, **29**, 1625; Gonnermann, Biochem. Ztschr., 1918, **88**, 401; Bertrand, Bull. Soc. hyg. aliment., 1920, **8**, 49; Winter and Bird, Jour. Amer. Chem. Soc., 1929, **51**, 2964.

[2] See U. S. Dep't. Agric. Bull. 103, 1914; "Hearings Docket 540, Federal Trade Commission vs. Royal Baking Powder Co."; "Trial Examiner's Report upon the Facts Concerning Alum in Baking Powder and Its Physiological Effects," New York, 1926; *The Truth about Baking Powder,* Chicago, 1927; *Aluminum Compounds in Food* by E. E. Smith, New York, 1928.

[3] Jour. Biol. Chem., 1928, **77**, 753; *Ibid.*, 1930, **85**, 779.

Myers and Killian[2], studying the solubility of aluminum compounds found in baking powder residues in the stomach and duodenum, showed that, with an ingestion of 15 to 90 mg. of aluminum, from 0.4 to 14.6 mg. have been found in the gastric contents in soluble form, the soluble aluminum, calculated on the basis of the amount actually present in the gastric contents, varying from 6 to 54 per cent., averaging about 25 per cent. Myers and Mull[3] show that minute traces of aluminum are present in the tissues normally and these increase only slightly on a diet containing considerable aluminum, the aluminum persisting in the tissues even on an aluminum-free diet. Following intraperitoneal administration, aluminum is found in increased amounts throughout the body, the largest amounts apparently being in the liver, while excretion appears to be chiefly through the intestine. For the liver the average findings of aluminum per 100 grams of tissue were: (1) control diet, 0.14 mg.; (2) aluminum diet, 0.18 mg.; (3) aluminum-free diet, 0.08 mg.; and (4) aluminum administered intraperitoneally, 8.22 mg. Myers and Morrison[4], in their investigations on the influence of administration of aluminum on the aluminum content of the tissues of the dog, found that aluminum is normally present in such tissues as the spleen, kidney, heart, and liver in amounts varying from 0.07 to 0.15 mg. per 100 grams, the largest amounts being present in the liver. After the daily ingestion of 0.23 and 1.55 grams of aluminum for 3 months, there was practically no change in the aluminum content of these same tissues, with the exception of the liver, where the amount averaged 0.27 mg. per 100 grams. They, also, showed that, when 5 mg. of aluminum were administered parenterally for 2 weeks, a marked increase in the aluminum content of the tissues was found 8 and 34 days after the administration had been discontinued, indicating that aluminum is slowly excreted. In their study of the aluminum content of human

[1] Science, 1929, **69**, 186; Jour., Biol. Chem., 1929, **83**, 261; *Ibid.*, 1930, **85**, 783.

[2] Jour. Biol. Chem., 1928, **78**, 591.

[3] Ibid., 605.

[4] Ibid., 615.

autopsy material, Myers and Mull[1] found that the higher figures were obtained with brain and heart tissue, the liver containing appreciably less. Thus, the average aluminum content, expressed in terms of mg. per 100 grams of tissue, are 0.25 mg. for brain, 0.21 mg. for the heart, 0.08 mg. for the liver, 0.10 mg. for the kidney, and 0.07 mg. for the spleen. Seibert and Wells[2] have shown that the daily intravenous injection into rabbits of small amounts of sodium aluminum sulphate produced a very definite secondary anemia and, at the site of the injection, local irritant effects, such as swelling, edema, inflammation and necrosis of the tissue and swelling of neighboring lymph nodes. Underhill and his associates[3] have confirmed the absorption of aluminum and the normal occurrence of this metal in the blood and tissues of animals and man. They find that aluminum is excreted through the walls of the gastro-intestinal tract at all levels. The pathologic lesions found following subcutaneous injection of salts of aluminum are largely in the liver and kidney, although the spleen shares these effects to some extent.

A further source of possible aluminum compounds in the system is in the ingestion of the small amounts arising from the dissolving of the metal from the cooking utensils by the acids or alkalies used in the cooking processes. That such action does lead to solution of some aluminum is undoubtedly true, yet Flinn and Inouye[4] state that "There is no scientific evidence of any chronic poisoning taking place from food cooked in aluminum utensils."

In spite of the somewhat unsettled state of the controversy concerning the harmfulness of the small amounts of aluminum compounds introduced into the gastro-intestinal tract of man, there is no question but that large doses of these derivatives do produce serious and fatal poisoning. Probably, the compound most frequently accountable for such poisoning is alum, by which is meant either the potassium-aluminum sulphate or the ammonium-aluminum sulphate, the sodium-aluminum sulphate not being regarded by some[5] as a true alum. Witthaus[6] has collected 7 such cases of fatal poisoning from large doses of alum, while reference is made to several non-fatal cases. Occasional cases of industrial poisoning of individuals working with heated aluminum have been reported[7], although Flinn and Inouye[8] do not classify aluminum as an industrial poison because of the absence of any evidence of chronic or acute poisoning in industrial plants.

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[1] Jour. Biol. Chem., 1928, **78,** 625.

[2] Arch. Path., 1929, **8,** 230.

[3] Underhill and Peterman, Amer. Jour. Physiol., 1929, **90,** 1, 15, 40, 52, and 62; Underhill, Peterman, Gross and Krause, Ibid., 67 and 72; Underhill, Peterman and Sperandeo, Ibid., 76.

[4] Jour. Amer. Med. Assoc., 1928, **90,** 1010.

[5] *The Current Significance of the Word Alum,* by Richardson, Chicago, 1927. See, however, Leffmann and Strock, Bull. Wagner Free Inst. Sci., 1928, **3,** 19.

[6] *Medical Jurisprudence, Forensic Medicine and Toxicology,* 1911, **4,** 273.

[7] See Spofforth, Lancet, 1921, **1,** 1301

[8] *Loc. cit.*

Symptoms.—On swallowing a solution of alum the patient complains of a burning pain in the mouth, throat and stomach. The mouth may look as if it has been tanned, owing to the marked astringent effect, while the irritating action on the stomach is evident in the repeated vomiting of bloody material (in one case reported by Kramolik[1] the patient vomiting 39 times in 48 hours). The pulse and respiration are accelerated, disturbances of coordination and clonic contractions of the muscles may be noted. In some cases evidences of marked nephritis are observed, in the form of dark colored urine containing blood, albumin and casts.

Fatal Dose and Fatal Period.—Thirty grams of alum have proven fatal in two cases, one in 8 hours[2] and one in 24 hours[3], although recovery has followed much larger doses.

Treatment.—The stomach should be washed out with copious quantities of water. Demulcent drinks of milk containing sodium carbonate may be given freely.

Postmortem Appearances.—The mucosa of the mouth, throat and esophagus may show signs of corrosion and some edema. The walls of the stomach appear contracted, the mucosa being somewhat hardened and showing areas of corrosion. The walls of the intestine are hyperemic. The liver may show fatty degeneration, while the kidney reveals parenchymatous degeneration.

Detection.—While traces of aluminum are probably always present in the tissues of the body and may be determined by the delicate method of Myers, Mull and Morrison[4], yet in cases of poisoning one may expect to find fairly large amounts deposited especially in the liver and spleen, and, according to the findings of Flinn and Inouye in their experimental animals, in large quantities in the bones. Kobert[5] has called attention to the finding of aluminum in prostatic concretions and in gall stones.

In the systematic process of examination of tissues, aluminum will be found in the filtrate from the hydrogen sulphide treatment of the acid solution obtained in the process of destruction of tissue by the method of Fresenius and von Babo, and this fluid may be used for the detection and determination of the amount of aluminum present. If it is desired to test directly for aluminum without going through the other steps, one may incinerate the tissues directly and take up the residue with dilute hydrochloric acid or employ the method of Schmidt and Hoagland[6]. If the fluid obtained in the systematic process is to be used, heat this to boiling to remove the hydrogen sulphide and filter. Concentrate the filtrate to a relatively small bulk, acidify with HCl, add a little ammonium chloride and follow this with ammonia to alkaline reaction, when any aluminum, iron, or chromium present will be precipitated, especially after the excess of ammonia is driven off by heat. Filter and wash the precipitate with water. Transfer the precipitate to a platinum or porcelain dish, and boil with an excess of sodium hydroxide solution, when the aluminum hydroxide will dissolve and the iron and chromium hydroxides will remain as insoluble residues. Filter, wash thoroughly with water, and treat the filtrate with an excess of ammonium chloride solution, when the aluminum hydroxide will again be precipitated in a quantitative manner. Now filter, wash with water, and dry the precipitate in the oven in the usual manner. Incinerate the filter and precipitate and weigh as aluminum oxide.

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[1] Pester Med.-chir. Presse, 1902, **38**, 241.

[2] See Gadamer, *Lehrbuch der chemischen Toxikologie*, 1924, p. 254.

[3] Hicquet, Bull. Soc. méd.-lég. de Paris, 1871, **2**, 428.

[4] Jour. Biol. Chem., 1928, **78**, 595.

[5] *Lehrbuch der Intoxikationen*, 2te. Aufl., 1906, **2**, 412.

[6] Jour. Biol. Chem., 1912, **11**, 387.

If it be desired to prove that this precipitate is actually aluminum oxide, the method of Hammett and Sottery[1] is especially valuable. Dissolve the precipitate in 5 cc. of N hydrochloric acid and add 5 cc. of 3 N ammonium acetate solution and 5 cc. of 0.1 per cent. solution of the ammonium salt of aurin-tricarboxylic acid. Mix and make the reddish lake alkaline with ammonium hydroxide containing some ammonium carbonate, when a bright red precipitate, which persists in the alkaline solution, indicates the presence of aluminum.

CHROMIUM

Of the compounds of chromium, chromic acid and its salts, the chromates and the bichromates, have the greatest interest from a toxicological standpoint, being about 100 times more toxic than the salts in which chromium exists as a kation rather than as an anion, that is than such salts as chromium chloride, chrome alum, and chrome green. Chromium trioxide or anhydride (CrO_3) is an official compound, occurring in small needle-shaped crystals or rhombic prisms of a dark purplish-red color and metallic luster. It is odorless and is deliquescent in moist air and is very soluble in water, forming chromic acid (H_2CrO_4). The oxide is very destructive to both animal and vegetable tissue and has found occasional use in medicine as an escharotic. The chromic acid is readily formed by the action of sulphuric acid upon potassium dichromate and exists, therefore, in battery fluids, which have occasionally caused serious burns and even general poisoning. The potassium chromate, K_2CrO_4, is a yellow salt readily soluble in water and is used in the manufacture of lead chromate (chrome yellow) and basic lead chromate (chrome red). The potassium and sodium bichromates are used in tanning, as mordants in dyeing and printing, in the manufacture of lead chromate, in oxidizing anthracene to make alizarin colors, and in photography and in photo-engraving." All of these compounds find frequent use in chemical processes in the laboratory.

Poisoning from chromic acid has occurred from its use as an escharotic applied to the tonsils, when some of it may be swallowed, or even from external application for removal of vegetations from the external genitalia;[1] and several deaths have occurred from swallowing battery fluid. Witthaus[2] has collected 28 reported cases of chromic acid poisoning, some of which were accidental and many of which were suicidal. Potassium chromate has caused poisoning in the human subject at least 4 times, while potassium bichromate has been reported as causing 67 cases of acute poisoning, according to Witthaus[3], of which 32 were suicidal, 22 accidental, 3 to procure abortion, 3 homicidal, and in 7 the origin is not stated. Since this summary of Witthaus, at least 12 accidental deaths occurred through a mistake of a pharmacist in Breslau[4]. Death from the lead chromates will be discussed later.

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[1] Jour. Amer. Chem. Soc., 1925, 47, 142.

Symptoms.—These usually appear suddenly within a few minutes. There is usually intense pain in the epigastrium and in the back, accompanied with violent and almost constant vomiting of material tinged with the poison taken (this color may be yellowish or bluish-grey or even green), later colored with blood and bile. These symptoms are often so marked that the patient is almost unable to perform any voluntary act. Diarrhea with occasional bloody stools, sensitive abdomen and marked abdominal pain follow. There may be precordial pain; the pulse is small and thready, and the respirations may be slow. Following this severe onset with symptoms of marked gastro-intestinal irritation, nervous symptoms soon appear in the form of vertigo, muscular cramps, unconsciousness and collapse. According to Kobert, if death does not occur in the first 10 hours, jaundice supervenes. The urine may show signs of nephritis.

Fatal Dose and Fatal Period.—The fatal dose of chromic acid is uncertain as far as reported cases go, although Gadamer[5] states that 6 grams has caused death. The smallest fatal dose of potassium bichromate for an adult appears to be between 2 and 3 grams taken by a man of 43 years with suicidal intent[6], death occurring in 10 days, while another case followed the ingestion of about 8 grams, death occurring in 10¾ hours.[7] Recovery has followed the taking of 17.7 grams.[8] According to Witthaus, in 20 out of 25 fatal cases, in which the duration of the poisoning is definitely stated, death occurred in 24 hours or less, with an average duration of 8¼ hours, although death has occurred in one case in 40 minutes[9] and in another in 50 minutes.[10]

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[1] See White, University Med. Mag., 1889, **2**, 54.

[2] *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 1911, **4**, 312.

[3] *Loc. cit.*, p. 702.

[4] See Jour. Amer. Med. Assoc., 1919, **73**, 1590; Brieger, Ztschr. f. exp. Path. & Therap., 1920, **21**, 393. Further, see Urban, Berl. klin. Wchnschr., 1919, **56**, 363; Colden, Ibid., 365; Jonsson, Hygiea, 1927, **89**, 84.

[5] *Lehrbuch der chemischen Toxikologie*, 1924, p. 244.

[6] Klimesh, Wien. klin. Wchnschr., 1889, **2**, 732.

[7] Gesenius, Deutsch. med. Wchnschr., 1882, **8**, 511.

[8] Philipson, Lancet, 1892, **1**, 138.

[9] Stewart, Brit. Med. Jour., 1888, **2**, 420.

[10] Waugh, Lancet, 1885, **2**, 1135.

Treatment.—The stomach should be freely washed out with water until the washings are no longer colored with the poison. Demulcent drinks, such as milk containing magnesium carbonate or sodium bicarbonate, should be given. Sedatives should be given for the pain, and respiratory and cerebral stimulants may prove of value in counteracting the nervous depression.

Postmortem Appearances.—The skin, the gums, and the internal organs may show a bluish-gray or a purplish-blue coloration due to the reduction of the chromate, although this change is by no means always present. The gastric mucosa, especially in the region of the fundus, shows evidences of inflammation, ecchymosis and swollen follicles. The intestines may be hyperemic, with ecchymoses here and there. The liver and heart may show fatty degeneration, while the kidneys give evidence of parenchymatous changes. The blood does not coagulate readily, and is brownish in color due to the presence of methemoblogin.

Chronic Poisoning.—Industrial workers in trades using potassium bichromate and chromic acid not infrequently suffer from the effects of local irritation of the skin and mucous membranes[1], which is slow and painless. It has been shown experimentally[2] that chromic acid, potassium bichromate and ammonium bichromate in solutions may readily produce skin irritation (dermatitis) without the necessity of any previous injury. Ulcers may form on the hands, arms, and other parts of the body and are especially noticeable in the nares, where they are large and indolent, slow to heal and are often accompanied by perforation of the septum.[3] It is probable that the inspiration of spray or mist in the atmosphere is the chief industrial hazard, the risk being in direct proportion to the concentration of chromic acid mist in the air and being greatly reduced by efficient ventilation.[4]

Detection.—Chromic preparations appear to be rather rapidly absorbed from the skin and gastro-intestinal tract and are excreted by the kidneys and bowel, while the liver seems to hold considerable of the absorbed chromium for a long period. The organs most likely to yield evidences of chromium poisoning are the liver and kidneys, although the stomach and bowels, as well as the urine, may contain appreciable amounts if death has been rapid.

If the tissues be treated by the method of Fresenius and von Babo for destruction of the organic matter, the liquid becomes green from the formation of chromic chloride, if chromium be present. If to the filtrate ammonium hydroxide be added in slight excess, chromic oxide will be precipitated. Filter, wash with water and dry the precipitate. If the precipitate be fused with a mixture of potassium nitrate and sodium carbonate, potassium chromate will be formed. Extract this fusion with warm water, filter and test for chromium as follows:

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[1] See Lehmann, Zentralbl. f. Gewerbehyg., 1914, **2**, 193.

[2] McCord, Higginbotham and McGuire, Jour. Amer. Med. Assoc., 1930, **94**, 1043.

[3] See Dixon, Jour. Amer. Med. Assoc., 1929, **93**, 837 for reports of 18 cases.

[4] See Bloomfield and Blum, Pub. Health Rep., 1928, **43**, 2330.

1. To the yellowish solution add sufficient acetic acid to acidify it and then add a solution of lead acetate, when a yellow precipitate of lead chromate forms, which is soluble in sodium or potassium hydroxide but not in ammonia.

2. Acidify the yellow solution with acetic acid and add silver nitrate solution, when a red precipitate of silver chromate forms, which is easily soluble in nitric acid and in ammonium hydroxide.

3. Acidify the yellow solution with hydrochloric acid, add a little alcohol and heat, when a green color appears in the presence of chromium.

Determination.—If quantitative determinations are to be made, the first steps in the process are the same as those given above. Make up the aqueous extract of the final fusion to a definite volume and take an aliquot part of this solution for the determination. Acidify this solution with acetic acid and precipitate with barium chloride solution, when a mixed precipitate of barium sulphate and barium chromate separates. Filter this precipitate through an asbestos filter and wash the precipitate free from nitrates. Place the asbestos mat containing the precipitate in a beaker, treat with concentrated sodium carbonate solution and heat. Filter this new precipitate through an asbestos mat and, if the residue of barium carbonate is not pure white, treat this again with sodium carbonate in the same manner. Evaporate the combined filtrates, containing the chromate in solution, to a small volume and place in a glass stoppered flask. Add 1 to 2 grams of potassium iodide and carefully acidify with hydrochloric acid. Allow the mixture to stand about 10 minutes to permit the iodine to separate out and titrate the iodine with N/10 sodium thiosulphate solution, using starch as an indicator. 1 cc. of the standard thiosulphate solution is equivalent to 0.049 gram of potassium bichromate or 0.00333 gram of chromic anhydride. According to Gadamer[1] the results of this method may be 5 to 10 per cent. too low.

ZINC

The metal zinc does not occur in nature as such, but exists in the form of such compounds as the carbonate, silicate and sulphide, most of which minerals may contain, also, some cadmium, lead, arsenic, antimony, and phosphorus as impurities. Zinc and its compounds appear to be widely distributed in various foods, in certain drinking waters, and in animal tissues, being especially noted in cereals, milk, eggs, oysters and many other marine animals, vegetables and most of the edible meats.[2] On account of this wide occurrence of zinc in the principal articles of food of man, it is not unexpected to find that zinc is to be regarded as a normal constituent of human tissues, as has been reported by various workers.[1] The ingestion of these small amounts over long periods of time results in accumulation in the tissues, especially in the liver, until the amounts become weighable[2], while the elimination takes place to a large extent through the gastro-intestinal tract and less through the urine. There appears to be little evidence that such amounts ever prove harmful to the organism, although some experimental work on animals, in which the zinc was introduced either by mouth or intravenously, showed some indications of renal injury along with a glycosuria and hyperglycemia, while other work along similar lines has shown that no pathological lesions follow from these small doses[3]. Mallory and Parker[4] reported the production of acute intracapillary glomerulonephritis as occurring in 4 out of 11 rabbits following the subcutaneous injection of 0.5 to 1 gram of metallic zinc in the form of fine powder. Further work with several zinc salts, as well as a repetition of the former experiments, has convinced these workers that no significant effect on the kidneys is produced by zinc and that the earlier results were due to spontaneous intracapillary glomerulonephritis and not to the action of zinc or its salts.[5]

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[1] *Lehrbuch der chemischen Toxikologie* 2te. Aufl., 1924, p. 248.

[2] In this connection see Javillier, Compt. rend. Acad. des Sci., 1907, **145**, 1212; These de Paris, 1908; Weitzel, Zentralbl. Physiol., 1914, **28**, 766; Rost und Weitzel, Arb. Reichsgesundsheitamt, 1919, **51**, 494; Birckner, Jour. Biol. Chem., 1919, **38**, 191; Hiltner and Wichmann, Ibid., 205; Rost, Die Umschau, 1920, **24**, 201; Bodansky, Jour. Biol. Chem., 1920, **44**, 399; Severy, Ibid., 1923, **55**, 79; Drinker and Collier, Jour. Ind. Hyg., 1926, **8**, 257; Bertrand and Benson, Am. de l'Inst. Pasteur, 1929, **43**, 386.

Zinc, both in the pure form and in the form of "galvanized iron", has been employed in the manufacture of cooking utensils, but it has been found that the use of such vessels may lead to the dissolving of so much zinc by the weak acids employed or generated in cooking that symptoms of systemic poisoning may arise. Thus Salkowski[6] has shown that a plum marmalade prepared in a vessel coated with zinc yielded 3.4 per cent. of zinc calculated as sulphate; while in an institution near London about 200 individuals were made acutely ill, with symptoms of dizziness, nausea, tightness in the throat, and, in some cases, diarrhea, from eating apples, which had been stewed in galvanized iron vessels. Analysis of the apples showed that they contained 7 grains of zinc, in the form of the oxide, to the pound.[7] Other food products, such as milk, vinegar, soup, olive oil and alcoholic liquids, may extract sufficient zinc to prove at least irritating, so that such vessels should not be used for cooking purposes.

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[1] See Van Itallie, Nederl, Tijdschr. v. Geneesk., 1919, **63**, 1709; Ghigliotto, Ann. de fals., 1919, **12**, 12; Giaya, Compt. rend. Acad. des Sci., 1920, **170**, 906; de Gramont, Ibid., 1037.

[2] See Salant, Rieger and Trenthardt, Jour. Biol. Chem., 1918, **34**, 463; Drinker, Fehnel and Marsh, Ibid., 1927, **72**, 375.

[3] See Sacher, Arb. a. d. r. Pharmakol. Inst. zu Dorpat, 1893, **9**, 88; Brandl and Scherpe, Arb. a. d. k. Gesundheitsamte, 1899, **15**, 185; Salant and Wise, Jour. Biol. Chem., 1918, **34**, 447; Salant, Jour. Ind. Hyg., 1920, **2**, 72; Heller and Burke, Jour. Biol. Chem., 1927, **74**, 85.

[4] Amer. Jour. Path., 1925, **1**, 541.

[5] Mallory and Parker, Ibid., 1927, **3**, 91.

[6] Zentralbl. der Biochemie und Biophysik, 1918, **19**, 345.

[7] See London letter, Jour. Amer. Med. Assoc., 1923, **80**, 707.

Zinc finds rather wide use in the industries, being employed in the manufacture of brass and other zinc alloys, in the making of galvanized iron, in the rubber and paint industries, and in the manufacture of certain kinds of paper, glass and dyes. Zinc is not regarded as an industrial poison by many authorities, although there can be little question that operators of oxyacetylene torches in working with bronze or galvanized metals or that brass founders do suffer with so-called "braziers' ague" or "brass founders' ague", characterized by irritation in the throat with painful cough, a feeling of lassitude and weariness, with slight pains and stiffness in the legs, followed by a severe chill with fever and accelerated pulse and respiration, and later by a feeling of exhaustion. Such conditions are possibly brought on by the inhalation of zinc oxide, as Lehmann[1] was able to produce the above train of symptoms by exposure to pure zinc fumes. It is doubtful, however, that these symptoms are actually the result of the poisonous action of zinc, *per se*, as Hamilton[2] points out. "An amount of zinc which, when administered as oxide through the air, will set up typical ague would, if injected in soluble form subcutaneously, hardly produce any noticeable symptoms. No other metallic poison produces an effect at all like brass-poisoning, which indeed resembles in some ways a bacterial infection with its incubation period, chills, fever, sweating, and sometimes evidence of widespread inflammation of the finer bronchioles." Hayhurst[3] believes that there is probably no such condition as chronic zinc or brass poisoning; while Flinn and Inouye[4] state that zinc is not classified as an industrial poison because of the absence of any evidence of chronic or acute poisoning in industrial plants. On the other hand, McCord and Friedlander[5] believe that zinc is capable of producing chronic systemic poisoning, characterized especially by widespread gastro-intestinal conditions, varying from gastro-enteritis to well established gastric and duodenal ulcers. These workers state that a long period of time (5 to 20 years) appears necessary for the production of such lesions and admit that other substances, such as lead, arsenic, or antimony, might be contributing factors.

The salts of zinc have found more or less use in medicine, the acetate, chloride, oxide, stearate, and sulphate being official. All of these, with the exception of the acetate, have been reported as the cause of poisoning. In 90 cases collected from the literature by Witthaus[6], the chloride was the cause of poisoning in 59, the sulphate in 29, the oxide in 1 and the sulphide in 1. Of the cases of poisoning with the chloride, 43 were accidental, 10 suicidal, and at least 3 were homicidal. In 32 of these cases some form of disinfecting fluid containing the chloride was used, as Burnett's fluid in 27, Crew's in 2, and Morell's in 1; while in 4 cases "soldering liquid" was swallowed. While most of these cases were the result of swallowing the chloride in some form or other, its use as a caustic has lead to absorption from the wounded surfaces with resulting death in at least 5 cases. In the case of the sulphate, 9 of the poisonings were the result of swallowing it in mistake for Epsom salts, in 8 instances it was taken with suicidal intent, in 1 to produce abortion, and in 5 it was given with homicidal intent. The widespread use of zinc stearate dusting powders has resulted in many deaths of infants by aspiration of the powder. Following the report of Heiman and Aschner[1] of 12 cases of accidental inspiration of this dusting powder, with resulting sudden and stormy bronchopneumonia with death, in one case, within one hour, the Committee of the American Medical Association has received, as a result of a request published in the Journal, reports of at least 131 cases, 28 of which terminated fatally.[2] The persistent collapse in these cases seemed strongly suggestive of a toxic effect, possibly a zinc poisoning, but it would seem that the action is not due to poisoning with zinc, as the symptoms are not those noted following inhalation of zinc oxide, but rather to the fact that the stearate is such a tenacious powder that an insufflation pneumonia is produced. The lesions produced by talcum powder are similar in kind but lesser in degree than those produced by zinc stearate, as pointed out by Heiman and Aschner, while pneumonic lesions have been produced by Meltzer and Kline[3] by the insufflation of unorganized substances.

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[1] Arch. f. Hyg., 1910, **72**, 358.

[2] "Industrial Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 779.

[3] See Kober and Hayhurst, *Industrial Health*, 1924, pp. 329, 333 & 342.

[4] Jour. Amer. Med. Assoc., 1928, **90**, 1010.

[5] Arch. Int. Med., 1926, **37**, 641.

[6] *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 1911, **4**, 782.

Symptoms.—The symptoms of poisoning depend, to some extent at least, on the salt of zinc taken. With the chloride, the action is especially that of a corrosive. The patient complains of a metallic, astringent taste in the mouth with almost instant burning pain in the mouth, throat and stomach. Vomiting usually follows in a short time, the matter ejected often containing blood. Swallowing is painful and there is a profuse flow of saliva. There is severe thirst, the countenance is pale and there is more or less aphonia. In a few minutes purging supervenes, associated with tenesmus and bloody stools. In rapidly fatal cases prostration may be great and the patient soon collapses, with coma and death in a few hours. In other cases, these symptoms may abate and nervous sequelae follow in the form of perversion of the special senses, localized tetanic contractions of groups of muscles, and great muscular weakness. A further group of cases may show a remission of the symptoms of corrosion and later signs of impaired digestion, inanition with extreme wasting and even death from the formation of strictures of the esophagus and pylorus. In the case of the sulphate, the symptoms are more those of gastro-intestinal irritation rather than of corrosion, as with the chloride. Zinc sulphate is rather frequently used as an emetic in doses of 1 to 1½ grams and usually acts promptly with little depression. However, in larger doses or, if some of it is retained, it acts as an irritant, producing pain in the mouth, throat and stomach, persistent vomiting, diarrhea, and prostration. There may be vertigo, syncope, convulsions, and collapse resulting in death. In rare cases, there may be little or no vomiting or purging, the symptoms then being almost entirely due to depression of the central nervous system followed by death.

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[1] Amer. Jour. Dis. Child., 1922, **23**, 503.

[2] See Jour. Amer. Med. Assoc., 1924, **83**, 120; Ibid., 1925, **84**, 750.

[3] Proc. Soc. Exper. Biol. & Med., 1915, **13**, 29.

Fatal Dose.—According to Witthaus[1] the smallest quantity of the chloride known to have caused the death of an adult was about 3.5 grams taken in the form of 2 drams of Burnett's solution[2], while Blyth[3] states that 0.38 gram has destroyed life after several weeks' illness, but cites no reference as to the case. In the case of a child, death has occurred following the taking of a teaspoonful of a 50 per cent. solution of the chloride (about 2 grams).[4] On the other hand recovery of an adult has followed the taking of 90 grams.[5] The smallest reported fatal dose of zinc sulphate appears to be 15.5 grams[6] taken by mouth, while 1 gram has proven fatal when given as an intrauterine injection,[7] Recovery has followed the taking of 46 grams[8]. The chloride appears to be more fatal than the sulphate, the percentage of fatal cases of the former being 65.8, while that of the latter is 50.

Fatal Period.—Death in 2 hours from the effects of Burnett's solution (zinc chloride) has been reported[9] while "soldering fluid" has proven fatal in 4½ hours[10]. The shortest duration of a case of zinc sulphate poisoning seems to be 2 hours after taking about 125 grams[11], while, in another case, death occurred in about 4 hours, no vomiting having taken place.[12] Death has been delayed for such long periods as six months[13] following the dose of the chloride, the fatal results being due to the inanition following stricture of the esophagus and pylorus.

Treatment.—While vomiting is usually present in cases of zinc poisoning, there are some cases in which it does not occur, so that the efforts of the stomach to remove the irritant should be assisted by administration of lukewarm water or milk. Emetics should not be given, but gastric lavage should be used to insure emptying of the stomach. Antidotes, such as milk, white of egg and strong tea should be given, followed by lavage. Pain may be controlled by opium if necessary, while stimulants should be given to counteract the symptoms of collapse.

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[1] *Medical Jurisprudence, Forensic Medicine and Toxicology* by Witthaus and Becker, 1911, **4,** 784.

[2] Cousins, Med. Times and Gaz., 1862, **2,** 404.

[3] *Poisons: Their Effects and Detection,* 4th ed., 1906, p. 691.

[4] Seydel, Vrtljschr. f. ger. Med., 1896, 3F., **11,** 286.

[5] Stratton, Edinb. Med. and Surg. Jour., 1848, **70,** 335.

[6] Marsh, Med. Times and Gaz., 1862, **2,** 252.

[7] Hofmeier, Monatschft. f. Geb. u. Gyn., 1896, **4,** 301.

[8] See *Forensic Medicine and Toxicology* by Woodman and Tidy, 1877, p. 226, Case 23.

[9] Brunton, Glasgow Med. Jour., 1869–70, 5s., **2,** 514.

[10] Crosse, Brit. Med. Jour., 1883, **2,** 820.

[11] Buchner, Friedreich's Bl. f. ger. Med., 1882, **33,** 255.

[12] Penfold, Austral. Med. Jour., 1883, n. s. **5,** 340.

[13] See Philosoph. Jour. and Trans., 1867, n. s. **8,** 420.

Postmortem Appearances.—The effects observed after death from zinc chloride are more marked than those following fatal doses of the sulphate. With the chloride one finds the mucous membrane of the mouth, throat and esophagus white, swollen and deprived of epithelium, while the gastric mucosa is usually softened and disintegrated at the cardiac end and that of the pyloric region more or less corrugated. If the case has not proven fatal for some days, ulceration and perforation may be noted. With the sulphate the evidences of irritation are present, but the effects are less severe than those noted with the chloride. Chronic poisoning with zinc salts causes a deposit of hemofuscin in the liver and the same type of lesion as does copper[1], but this point will be discussed later.

Detection.—In cases of poisoning by zinc, the elimination is largely through the gastrointestinal tract, less being excreted in the urine. It is to be expected, therefore, that the stomach and intestines with their contents would show zinc in the larger quantities, although other organs would yield their quota. Thus, in a case investigated by Barral[2], the blood showed 6 mg.; stomach 16 mg.; intestines 56 mg.; liver 28 mg.; brain 38 mg.; and feces 166 mg. per kilo. He rightly calls attention to the fact that little importance should be attached to the finding of small amounts of zinc in the tissues, as the normal zinc varies, according to different authors, from 10 to 45 mg. per kilo of tissue. It is to be recalled that in some cases zinc may be introduced into the body in an embalming fluid, although few of such fluids now contain zinc.

In the systematic process of examination of tissues for inorganic poisons, zinc will be found in the filtrate from the H_2S precipitation of the heavy metals and may be detected by the usual methods of qualitative analysis. Especially serviceable tests for zinc are (1) precipitation of white zinc sulphide from an alkaline or neutral solution by either hydrogen sulphide or ammonium sulphide. This precipitate is soluble in mineral acids but not in acetic acid. Owing to the presence of other inorganic ions in the solution to be tested, the sulphide may not show a pure white color, so that it should be purified by dissolving in nitric acid, evaporating to dryness, dissolving the residue in dilute HCl, alkalinizing with ammonia, filtering off the precipitated iron hydroxide, acidifying the filtrate with acetic acid and passing H_2S, when the zinc sulphide should appear as a pure white precipitate; (2) addition of a solution of potassium ferrocyanide to the hydrochloric acid solution of a suspected zinc salt throws down a gelatinous white precipitate of zinc ferrocyanide, which is soluble in excess of the precipitant and only sparingly soluble in HCl.

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[1] Mallory, Amer. Jour. Pathol., 1925, **1**, 129.

[2] Ann. de méd. lég. de criminol. et de police sci., 1928, **8**, 3.

If this precipitate be treated with a little bromine water, a deep yellow oxidation product is obtained.

Determination.—If zinc has been shown by the qualitative tests, the amount present may then be determined as follows: Weigh out 100 grams of the finely hashed material, mix with water and destroy the organic matter by the method of Fresenius and von Babo or, if preferred by the Gautier method. After the usual procedure for removal of the metals precipitable by H_2S in hydrochloric acid solution, as outlined on page 341, boil the filtrate to expel H_2S and filter from any sulphur that may separate. Add a drop of methyl orange indicator and 5 grams of ammonium chloride, and make the filtrate alkaline with strong ammonium hydroxide. Add dilute hydrochloric acid (1 to 9), drop by drop, until the reaction is faintly acid, add 10 to 15 cc. of 50 per cent. sodium or ammonium acetate solution, and pass in H_2S until precipitation is complete. Allow the precipitate to settle, filter and refilter if necessary until the filtrate is clear, washing the precipitate twice with hydrogen sulphide water. Dissolve the precipitate on the filter with a little dilute hydrochloric acid (1 to 3), wash the filter with water, boil the combined filtrate and washings to expel H_2S, cool, and add a distinct excess of bromine water. Now add 5 grams of ammonium chloride and ammonium hydroxide until the color, caused by the free bromine, disappears. Add dilute HCl.(1 to 3), drop by drop, until the bromine color just reappears; then add 10 to 15 cc. of sodium or ammonium acetate solution and 0.5 cc. of 10 per cent. ferric chloride solution, or enough to precipitate all the phosphates. Boil until all the iron is precipitated. Filter while hot and wash the precipitate with water containing a little sodium acetate. Pass H_2S into the combined filtrate and washings until all the zinc sulphide, which should be pure white, is precipitated. Filter upon a weighed Gooch filter previously heated to constant weight, wash the precipitate with hydrogen sulphide water containing a little ammonium nitrate. Dry the crucible and its contents in an oven, ignite at a bright red heat, cool and weigh as zinc oxide.[1]

MANGANESE

Manganese is found in the native state only in meteorites, but occurs rather widely distributed in the form of its various oxides and the sulphide. It is apparently taken up by plants from the ground and is introduced into the system of animals, being found in most tissues. Bertrand and Medigreceanu[2] have shown the constant presence of manganese in the blood and tissues of various animals, while Reiman and Minot[3], using a very sensitive method, have found that human blood contains from 0.004 to 0.02 mg. of manganese per 100 grams, while practically all human tissues show varying amounts, the liver yielding the highest figures with an average of 0.17 mg. per 100 grams of wet tissue. Headden[1] showed that wheat contained about 40 parts of manganese per thousand of dry matter, while Jones and Bullis[2] report its presence in the common leguminous plants. Recently Titus and Cave[3] report that manganese exerts a very beneficial effect upon anemia of rats and rabbits and seems to have some influence upon hemoglobin formation.

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[1] *Official and Tentative Methods of Analysis of the Association of Official Agricultural Chemists*, 2nd ed., 1925, p 175.

[2] Ann. Inst. Pasteur. 1912, **26**, 1013; Ibid., 1913, **27**, 1 and 282.

[3] Jour. Biol. Chem., 1920, **42**, 329.

While the soluble salts of manganese are all toxic, very few cases of acute manganese poisoning have been reported. At least three cases of fatal acute poisoning with potassium permanganate have been reported,[4] in which death was due to the marked corrosive action on the throat resulting in edema of the glottis. Numerous reports of the irritating gastric action of this salt may be found in the literature, but, so far as we have been able to find, death has not occurred in such cases.

The most important form of manganese poisoning is that occurring in workers in manganese ores and in those exposed to the fumes of manganese dioxide in separating mills, the symptoms being due to chronic poisoning and related almost entirely to the nervous system. This condition was apparently first described by Couper[5] and has been later discussed by several writers in Europe, where 15 cases have been reported. In America some 56 cases are found in the literature, all presenting the symptom-complex previously observed in the European workers.[6]

Symptoms.—In the reported cases of acute poisoning, all of which were suicidal, the symptoms have been almost entirely related to the irritation and corrosion in the throat with resulting edema. In non-fatal cases, potassium permanganate in somewhat large doses produces gastric irritation with pain, nausea and vomiting. After absorption, the nervous symptoms are noted.

In the chronic type the symptoms of reported cases as summarized by Edsall, Wilbur and Drinker are as follows: Following a history of exposure to manganese dust for at least three months, there is noted languor and sleepiness; stolid, mask-like facies; low, monotonous voice with economical speech; muscular twitching varying in degree from a fine tremor of the hands to gross rhythmic movements of the arms, legs, trunk and head; cramps and stiffness in the calfs usually at night; slight increase in tendon reflexes, ankle and patella clonus, Romberg sign inconstant; retropulsion and propulsion; peculiar slapping gait, the patient keeping as broad a base as possible to avoid propulsion; occasionally uncontrollable laughter, less frequently crying; absence of sensory, rectal, genito-urinary, or gastro-intestinal disturbances, of eye changes, of reactions of degeneration, of blood, urine and spinal fluid alterations. Gayle noted paresthesias as an early complaint in four of his cases, while all of his cases showed abnormal mental symptoms, especially of the personality.

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[1] Jour. Agr. Res., 1915, **5**, 349.

[2] Jour. Ind. and Eng. Chem., 1921, **13**, 524.

[3] Science, 1928, **68**, 410. See, also, Titus, Cave and Hughes, Jour. Biol. Chem., 1928, **80**, 565; Titus and Hughes, Ibid., 1929, **83**, 463.

[4] See Thomson, St. Petersb. med. Wchnschr., 1895, N. F. **12**, 329; Box and Buzzard, Lancet., 1899, 2, 411; Adler, Med. Klinik, 1914, **10**, 1386.

[5] Jour. de clin. méd., de pharm., at de toxicol., 1837, **3**, 223. See, also, von Jaksch, Wien. klin. Rundschau, 1901, p. 729; Embden, Deutsch. med. Wchnschr., 1901, **27**, 795; Seelert, Monatschr. f. Psychiat. u. Neurol., 1913, **34**, 82.

[6] See Casamajor, Jour. Amer. Med. Assoc., 1913, **60**, 646; Edsall, Wilbur and Drinker, Jour. Ind. Hyg., 1919, **1**, 183; Davis and Huey, Ibid., 1921, **3**, 231; Gayle, Jour. Amer. Med. Assoc., 1925, **85**, 2008.

Fatal Dose and Fatal Period.—In Adler's case of $KMnO_4$ poisoning, 10 grams proved fatal on the fourth day, while in Thomson's case, between 10 and 20 grams caused death in 6 hours, and in the case of Box and Buzzard an unknown amount killed in 35 minutes. In the chronic cases, the prognosis as to life is good, no fatal cases being directly traceable to the manganese poisoning. However, no case of recovery from the paralysis is recorded.

Treatment.—In the acute cases, prompt gastric lavage and administration of milk and white of egg should be followed. The symptoms should be combated as they arise. In the chronic types of manganese poisoning, treatment is of no value. All workers in manganese plants should be protected against inhalation of the dust, although by no means all workmen exposed contract the poisoning, a special susceptibility and long exposure being essential.

Postmortem Appearances.—In the acute cases reported, the autopsy findings were almost entirely associated with the corrosion and swelling of the buccal and laryngeal structures. No signs of gastro-intestinal irritation were noted. In the experimental cases in animals, Handovsky, Schulz and Staemmler[1] observed fatty changes in the cells of the liver and at times in the kidney and heart; and a destruction of red blood cells as indicated by the formation of hemosiderin. These workers report that the amount of manganese in the different organs in fatal poisoning is not necessarily related to anatomical changes in the organs.

Detection.—Manganese is eliminated from the body largely through the feces and bile, although the urine may contain faint traces. McCrackan and Passamaneck[2] have reported a study of the urine in 5 cases of chronic manganese poisoning and found traces in 3 of these cases, using a modified method which is very delicate. Manganese appears to be deposited in most of the tissues in varying amounts, especially in the bones, liver, spleen and brain, while the fecal material may give good yields. Owing to the normal presence of traces of manganese in the organs, the detection of such traces has no significance in toxicological cases, so that quantitative estimations must be made in suspected cases. As manganese has so little actual toxicologic interest, the methods for its detection and determination will not be discussed.

[1] Arch. exp. Path. u. Pharm., 1926, **110,** 265.

[2] Arch. Path. and Lab. Med., 1926, **1,** 585.

SILVER

Silver is fairly widespread in the mineral kingdom and finds extensive use in the arts and industries. Its salts are employed in cosmetics and in hair dyes, while the nitrate has been frequently used as a local caustic. In organic combination with protein material and, also, in the colloidal form it is extensively employed for its bactericidal powers, such preparations as protargol, argyrol, silvol, etc. finding wide application. These colloidal preparations correspond to the official substances *Argento-Proteinum Forte* (strong silver-protein) and *Argento-Proteinum Mite* (mild silver-protein), the former being a compound of silver and protein containing not less than 7.5 and not more than 8.5 per cent. of silver, while the latter contains not less than 19 and not more than 25 per cent. of silver.

Probably the only salt of silver that has caused poisoning is the nitrate, owing to its wide use in medicine, yet any of the soluble salts would probably show the same toxicity. Silver nitrate is official in the form of colorless, odorless, transparent, tabular, rhombic crystals very readily soluble in water; and, also, in the form of *Argenti Nitras Fusus* (lunar caustic, *lapis infernalis*), a white, hard, odorless solid, generally in the form of pencils or cones. Of the 8 cases of acute silver nitrate poisoning collected from the literature by Witthaus[1] 5 were the result of accident in children, only one of which was fatal, and 3 were in adults, 2 of which were fatal.

Symptoms.—In acute cases silver nitrate acts as an astringent and corrosive. Unless there is immediate vomiting of the material ingested, there is instant pain and burning in the throat and stomach, followed by vomiting of white masses, which darken on exposure to light, and later purging of bloody material. After absorption occurs, vertigo, paresis, and complete paralysis of certain groups of muscles, labored respiration and coma, followed by death from paralysis of respiration or from edema of the lungs may be noted.

Long continued use of either organic or inorganic silver preparations, or continuous working with silver and silver oxide leads to a chronic type of poisoning characterized by a peculiar, grayish-blue or black, indelible color of the skin, especially of those parts exposed to the light. This condition is known as argyria and may be (1) local, if the silver be deposited locally at the site of entrance, or (2) generalized, following absorption and transportation through the blood and lymphatic systems. In this latter form of argyria, the portal of entry of the silver is usually the gastro-intestinal tract, although some may be absorbed from mucous membranes to which it may be applied, and cases have been reported of absorption through the body surface. The first appearance of generalized argyria occurs usually over the edges of the gums in the form of a bluish-violet margin, although some cases may show the first appearance around the finger nails. Following the appearance of the blue line along the gums, similar discolorations develop over the mucous membranes of the mouth, conjunctivae, sclerae and skin of the face, and, later, the bluish color may extend to the entire surface of the body, the exposed parts showing a more intense coloration than the covered areas. The gum-line has been noted after a two months' treatment of a patient with silver nitrate, the total amount taken being 3.9 grams; while the color of the skin seems to arise only after relatively large doses.[1] In 800 silver workers in Berlin, patches of discoloration were found, which were attributed to absorption through abrasions of the hands.[2] Local application of organic silver compounds, such as collargol and argyrol, has lead to generalized argyria.[3]

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[1] *Toxicology*, 1911, p. 304.

Fatal Dose and Fatal Period.—This has not been definitely determined. According to Holland[4] death has resulted from 30 grains of silver nitrate taken by an adult, but, as no reference to the literature is given, we have been unable to confirm the statement. Recovery has followed the taking of 30 grams.[5] In the case reported by Scattergood[6], a child of 15 months of age died in 6 hours after swallowing a piece of silver nitrate about ¾ inch long. While the symptoms of poisoning usually come on rapidly, yet death is usually deferred for 24 or 48 hours or longer.

Treatment.—The antidotes of value in silver nitrate poisoning are sodium chloride, to form the insoluble silver chloride, and tannic acid to form insoluble silver tannate. These should be followed by washing out the stomach with large amounts of water, as the silver chloride is soluble in excess of sodium chloride and, also, as the silver albuminate present in the stomach is soluble in the salt solution. Milk and eggs may be given to promote the formation of silver albuminate. Attempts to remove the discolorations noted in argyria have not been very successful. Stillians and Lawless[7], however, have found that the intradermal injection of a mixture of 1 per cent. potassium ferricyanide solution with 6 per cent. sodium thiosulphate solution removes a large part of the silver from the skin in old cases of argyria with deep pigmentation, the blue color disappearing most easily.

Postmortem Appearances.—In the acute cases, there is coagulation of the protein of the superficial layers of the mucous membranes of the throat and esophagus resulting in a white stain, which turns black on exposure to the air. The signs of local irritation and corrosion are present in the stomach and bowels. In the chronic cases, pigmentation of the skin and internal organs with deposits of silver, probably organic in nature (albuminate), is characteristic, practically all organs of the body, with exception of the brain and cord, being involved. The silver seems to have a special affinity for connective tissue and, particularly, for the elastic fibers, in the connective tissue the silver rarely being in the cells, but deposited between the bundles of collagen and the elastic fibers[1]. In the skin these deposits are in the form of fine grains in the upper layer of the corium, as well as in the deeper connective tissue.

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[1] Myers, Amer. Jour. Syph., 1923, **7**, 125; Firth and Harrison, Brit. Jour. Dermat. and Syph., 1924, **36**, 105.

[2] See Brit. Med. Jour., 1887, **2**, 321.

[3] See Crispin, Jour. Amer. Med. Assoc., 1914, **62**, 1394; Goldstein, Ibid., 1921, **77**, 1514; Tobler, Schweiz. med. Wchnschr., 1922, **52**, 774; and Davis, Virginia Med. Month., 1924, **51**, 154.

[4] "Inorganic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 175.

[5] Orfila, *Traitè de toxicologie*, 5éme ed., 1852, **2**, 22.

[6] Brit. Med. Jour., 1871, **1**, 527.

[7] Arch. Dermat. and Syph., 1928, **17**, 153; and Jour. Amer. Med. Assoc., 1929, **92**, 20.

Detection.—In the systematic analysis of tissues for mineral poisons, the silver will be found partly in the insoluble residue from the treatment with hydrochloric acid and potassium chlorate, and partly in the filtrate from this residue, if the Fresenius and von Babo method be employed. If Gautier's method is used, the silver will largely be in solution in the form of silver nitrate, although some will, probably, be found in the insoluble residue, in the form of silver chloride, or, possibly, metallic silver. Qualitative tests of these different portions will reveal the presence of silver.

For the quantitative determination we follow the method outlined by Gettler, Rhoads, and Weiss[2], which is as follows. Weigh out definite amounts of the tissue, acidify with nitric acid, dry and ash in an electric furnace at a dull red heat. Leach this ash with hot water in order to extract all soluble silver salts. Filter and leach the residue with ammonia water to dissolve any silver chloride and silver phosphate present. Filter and digest the residue with hot nitric acid to dissolve all metallic silver. Filter this solution. Combine the three solutions, and, if the mixed filtrates are not alkaline, alkalinize with ammonia. Now add hydrochloric acid, gradually and with constant stirring, until all the silver is precipitated, making the final solution slightly acid with HCl. Place this acid fluid containing the precipitated silver chloride in a boiling water-bath for 1 hour and allow it to stand in the dark for 24 hours. Filter off the precipitate, wash several times with water containing a little nitric acid, redissolve the precipitate with ammonia water, and treat the alkaline solution with hydrogen sulphide. Filter off the precipitate of silver sulphide, and wash it with water. This precipitate of silver sulphide is then dissolved in concentrated nitric acid, and the solution evaporated to dryness on a boiling water-bath. This residue is dissolved in water, and, if not perfectly clear, is filtered, the filter paper being washed thoroughly and the washings being added to the main solution. This solution is now acidified with nitric acid and brought to a boil. Hydrochloric acid is now added drop by drop, with stirring, until all the silver is completely precipitated. Allow this precipitate to stand in the dark for 24 hours, after which filter it through a weighed Gooch filter, wash with water containing a little nitric acid, until the filtrate is free from HCl, and finally wash twice with alcohol. Dry at 100°C., and finally at 130°C., to constant weight. To obtain the amount of silver as such, multiply the weight of the silver chloride obtained by 0.7527.

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[1] Gettler, Rhoads, and Weiss, Amer. Jour. Path., 1927, **3**, 631.

[2] *Loc. cit.*

LEAD

Lead is, probably, the most important of the metallic poisons and has, no doubt, been accountable for more industrial poisonings than any other element. Practically all forms of lead are poisonous, even the metal itself. The basic carbonate and the suboxide (Pb_2O) are, probably, the most dangerous of the lead compounds, although the higher oxides, litharge (PbO) and red lead (Pb_3O_4), are frequent sources of poisoning. It has been shown that the proportion of those suffering from lead encephalopathy is higher in the industries employing lead oxides than in any other branch of the lead industry,[1] a fact that may be related to the relative solubility of these oxides in blood serum as shown by Fairhall.[2] The sulphate, chromate and sulphide are less toxic than the above-mentioned lead compounds, although all of these must be regarded as dangerous, owing to their solubility in human gastric juice and the resultant capability of absorption.[3] The water-soluble lead compounds, the acetate, chloride and nitrate, are toxic, but figure more in cases of acute than in industrial cases of lead poisoning.

While cases of acute lead poisoning are not especially frequent, yet Witthaus[4] finds recorded 124 cases, of which 44 were fatal, 10 being supposedly homicidal, 33 non-homicidal, and 1 doubtful.

The chronic type of lead poisoning is of great medical and hygienic importance, as the number of cases occurring in industry each year is very great, while many non-industrial chronic poisonings are observed. In the handling of lead ores in mining, in the sampling and smelting of the ore, in the manufacture of white lead by either the old Dutch or the Carter processes, in pottery glazing, in the making of storage batteries, in japanning and enameling, in shot and bullet making, and in the color-grinding, painting, plumbing and printing trades, lead in one form or another may be introduced into the system by inhalation or through food and drink contaminated by unclean hands. Lead may gain entrance into the body through the skin in the handling of pig-lead or leaden objects[5] and, also, by inhalation of the fumes arising from molten lead[6] in the case of solderers, lead-burners and makers of leaden objects. Hamilton found in Illinois 70 industrial processes which had given rise to lead poisoning[1], while Layet[2] computed that in France 111 industrial processes involved the use of lead.

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[1] Legge and Goadby, *Lead Poisoning and Lead Absorption*, 1912, p. 249.

[2] Jour. Biol. Chem., 1924, **60**, 481.

[3] See Carlson and Woelfel, Jour. Pharmacol. and Exp. Therap., 1913, **5**, 549.

[4] *Medical Jurisprudence, Legal Medicine and Toxicology* by Witthaus and Becker, 1911, **4**, 717.

[5] See Shie, Jour. Amer. Med. Assoc., 1921, **76**, 835.

[6] See Roth, Beitr. z. path. Anat. u. allgem. Path., 1905, **7**, Supp., 184; and Phelps, *Hygiene of the Printer's Trade*, U. S. Bureau of Labor Statistics, Bull. 209. 1917, p. 14.

By no means all of the chronic or subacute cases of lead poisoning are found in the industries. So-called "epidemics" of lead poisoning have occurred from drinking water contaminated by the lead from the pipes through which the water flows[3]. We find cases arising from drinking beer brewed in lead lined vats, or from wine contaminated by lead. Lead may be introduced into food in the cooking processes by the use of leaden vessels, while some food-products are colored with such lead compounds as the chromate and vegetables and fruit (such as apples) may be contaminated by being sprayed with lead arsenate. In the case of nursing infants, lead poisoning has occurred from the milk excreted by mothers using lead-containing cosmetics and hair dyes, as reported by Dufour.[4] Suzuki and Kaneko[5] report that the long observed serous meningitis in Japanese infants is due to white lead powders used as cosmetics by the mothers; while Fukushima and Matsumoto[6] state that of 298 children admitted to the Kyoto hospital with lead poisoning due to this cause, 215 (72 per cent.) died. A rather frequent cause of lead poisoning in children is found in their morbid craving to gnaw painted objects, such as window sills, white furniture, crib railings, etc. This craving for unnatural articles of food (pica) is responsible for two cases reported by Ruddock[7], while the introduction of lead into the mouth with resulting poisoning has occurred from lead stoppers of nursing bottles, from rubber nipples containing lead and from lead nipple shields.[8] Further, lead poisoning has arisen from bullets embedded in the tissues, and cases have been reported from the swallowing of shot.[9] A peculiar cause of lead poisoning is found in the contamination of snuff by the lead-foil wrapping of the packages, some 34 cases of which are found in the literature.[10]

Another industrial hazard was introduced in 1923, when gasoline containing tetra-ethyl lead was placed on the market. This compound

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[1] Jour. Amer. Med. Assoc., 1911, **56**, 1241. In this connection see, also, Dean, Jour. Ind. Hyg., 1924, **6**, 245; Hamilton, Jour. Amer. Med. Assoc., 1924, **83**, 583; *Industrial Poisons in the United States,* 1925; Leathers and Morgan, Jour. Amer. Med. Assoc., 1927, **89**, 1107.

[2] Cited by Rosenau, *Preventive Medicine and Hygiene,* 5th ed. 1927, p. 1241.

[3] See Hoffman, "Deaths from Lead Poisoning," U. S. Bureau of Labor Statistics, Bull. 426, 1927; Rigot and Emeric, Rev. d'hyg., 1927, **49**, 259.; Seitz, Münch. med. Wchnschr., 1927, **74**, 1364; Wright, Sappington and Rantoul, Jour. Ind. Hyg., 1928, **10**, 234.

[4] Thèse de Paris, 1901.

[5] Jour. Oriental Med., 1924, **2**, 55; abstract in Jour. Amer. Med. Assoc., 1924, **82**, 1819.

[6] Oriental Jour. Dis. Infants, 1928, **3**, 27; abstract in Jour. Amer. Med. Assoc., 1928, **90**, 1515.

[7] Jour. Amer. Med. Assoc., 1924, **82**, 1682.

[8] See Wilcox and Caffey, Jour. Amer. Med. Assoc., 1926, **86**, 1514.

[9] See Lewin, Arch. f. klin. Chir., 1910–11, **94**, 937; and Campaner, Rev. Esp. de Med. y. Cir., 1924, **7**, 328.

[10] See Uttal, Jour. Amer. Med. Assoc., 1928, **90**, 288; Bauer and Ropes, Ibid., 757.

($Pb(C_2H_5)_4$) was added to gasoline to eliminate the "knock" or detonation in automobile engines. A halogen carrier, either ethylene dibromide or trichlorethylene, is added, and during combustion decomposition of the tetra-ethyl lead occurs, with the formation of lead chloride or bromide, along with lead sulphate formed from the sulphur in the gasoline and, also, small amounts of lead oxide and metallic lead. From the report of Eldridge[1], it is clear that tetra-ethyl lead can be absorbed through the skin and the respiratory tract, and that there is a cumulative effect when repeated sublethal doses are administered. He says: "It is quite evident from these observations that the manufacture, handling and distribution of lead tetra-ethyl involves considerable danger to operatives, of acute lead poisoning in those instances where considerable material is splashed upon the skin, and of chronic lead poisoning from the absorption of small amounts by inhalation, by the skin or by the mouth." That this hazard in the manufacturing of this lead compound is a real one is shown by the fact that some seventy cases of poisoning have occurred, eleven men dying and one becoming insane from the effects of tetra-ethyl lead.[2] A further hazard falls to the lot of the men handling the ethyl fluid in mixing it with gasoline and to the employees of filling and distributing stations, as well as to the public at large, as the fluid may be splashed upon the hands or face and be rapidly absorbed through the skin. From the general standpoint, however, the greatest hazard to the greatest numbers may, possibly, be found in the exhaust gases from engines using ethyl gasoline. These exhaust gases contain lead compounds in the form of more or less fine dust, which partly passes into the air and partly cakes the exhaust pipes and later finds its way into the streets in the form of scales, inhalation of which might result in chronic lead poisoning from repeated small doses. In a report made by the United States Bureau of Mines in 1924, it was shown that tetra-ethyl lead in gasoline gives an average of less than half the amount of carbon monoxide found in the average automobile exhaust gas. This report apparently "indicates seeming remoteness of any danger of undue lead accumulation in the streets through the discharging of scale from automobile motors", and concludes that "the only danger of lead poisoning from products of combustion of ethyl gasoline seems to be confined possibly to the mechanic who is continually cleaning carbon from motors." While this report was issued by a government agency and would seem to carry some finality with it, yet Drinker and Edsall[3] believe that the material is presented in too insufficient detail, while Hamilton, Reznikoff and Burnham[4] "believe that these conclusions are not warranted and that the evidence so far available seems to show a real danger of chronic lead poisoning connected with garage work when ethyl gasoline is used and a possible danger to the public from lead dust in the streets of large cities."

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[1] "A Study of the Toxicity of Lead Tetra-Ethyl", Report 29, Chemical Warfare Service, 1924.

[2] See Hamilton, Reznikoff and Burnham, Jour. Amer. Med. Assoc., 1925, **84**, 1481.

[3] Jour. Indus. Hyg., 1925, **7**, 94.

[4] Jour. Amer. Med. Assoc., 1925, **84**, 1481.

Under date of January 17, 1926 a Special Advisory Committee[1] made its report, containing the following conclusions reached after careful consideration of an extensive series of tests under the direction of Dr. J. P. Leake of the Public Health Service:

"1. Drivers of cars using ethyl gasoline as a fuel and in which the concentration of tetra-ethyl lead was not greater than one part to 1300 parts by volume of gasoline, showed no definite signs of lead absorption after exposure approximating two years.

"2. Employees of garages engaged in the handling and repairing of automobiles and employees of automobile service stations may show evidence of lead absorption and storage, as indicated by the lead content of the feces and the appearance of stippled cells in the blood. In garages and stations in which ethyl gasoline was used the amount of apparent absorption and storage was somewhat increased, but the effect was slight in comparison with that shown by workers in other industries when there was a severe lead hazard (Group E) and for the periods of exposure studied was not sufficient to produce detectible symptoms of lead poisoning.

"3. In the regions in which ethyl gasoline has been used to the greatest extent as a motor fuel for a period of between two and three years, no definite cases have been discovered of recognizable lead poisoning or other disease resulting from the use of ethyl gasoline.

"In view of these conclusions your committee begs to report that in their opinion there are at present no good grounds for prohibiting the use of ethyl gasoline of the composition specified, as a motor fuel, provided that its distribution and use are controlled by proper regulations."

The Committee admits, however, that the experiments upon which the report is based may not have been extensive enough and that a dangerous hazard may arise, should the use of ethyl gasoline become widespread.[2]

As the toxicity of tetra-ethyl lead has been shown by Kehoe[3] to be a function of its lead content, it is interesting to note that Armstrong[4] believes that this compound is not dangerous primarily as a lead poison but as a poison in itself acting as a whole. In connection with the work, upon which the report of the Committee above-mentioned was based, it was found that there was a considerable proportion of lead in the dust of garages, even when ethyl gasoline had not been used therein, this lead amounting to as much as ⅓ mg. to 10 cubic meters of air or in settled dust to as much as 1 per cent. of the inorganic matter. Further evidence of this lead was, also, shown by the presence of lead in the feces of the garage workers, who had not been exposed to ethyl gasoline, and in the slight increase in the stippling of the red cells of such workers. In a further investigation Leake[1] has found in various industrial dusts, in which there was no evidence of lead hazard, about the same amount of lead as in the garages. In a series of examinations of the excretion of lead by 65 apparently normal, healthy workmen, who were chosen at random and were not exposed to lead hazard, all of the subjects studied were excreting lead either in the urine or feces, and in most instances in both.[2]

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[1] The manufacturers of ethyl gasoline voluntarily stopped the sale of this product on May 5, 1925. At a conference called by Surgeon General Cumming of the U. S. Public Health Service, a Special Advisory Committee was appointed, consisting of Dr. W. H. Howell, Chairman, Dr. David Edsall, Prof. C. E. A. Winslow, Dr. W. S. Leathers, Dr. A. J. Chesley, Dr. Julius Stieglitz, and Prof. Reid Hunt, to determine whether or not there is a public health hazard involved in the manufacture and use of tetra-ethyl lead gasoline.

[2] See Jour. Amer. Med. Assoc., 1926, **86,** 370; Jour. Indus. Hyg. 1926, **18,** 193; "The Use of Tetra-Ethyl Lead Gasoline in Its Relation to Public Health", U. S. Public Health Service, Bull. 163, 1926.

[3] Jour. Lab. & Clin. Med., 1927, **12,** 554.

[4] London Letter, Jour. Amer. Med. Assoc., 1928, **91,** 1387.

Absorption and Elimination.—Lead is absorbed from the respiratory tract, from the gastro-intestinal tract, and through the skin. It is probable that the inhalation of lead dust constitutes the most serious industrial hazard, although the ingestion of lead compounds into the stomach is, probably, accountable for the majority of the cases of non-industrial lead poisoning, while absorption through the skin is possible from paints, cosmetics, hair dyes, and, especially, from tetra-ethyl lead.

Absorption from the respiratory tract takes place all along the tract, the lead being directly absorbed into the circulation and carried to all the tissues. For this reason we find that the most acute and serious cases of lead poisoning follow exposure to dust and fumes. With absorption from the gastro-intestinal tract, the absorbed lead is carried through the portal circulation to the liver, which organ takes out or holds back a large part of the lead and thus prevents its rapid passage into the general circulation. In other words, "When lead enters the body by way of the respiratory tract, both absorption and excretion involve transportation in the systemic blood; while lead entering through the gastro-intestinal tract may be excreted without being absorbed, or after absorption may be caught by the liver and excreted in the bile without ever reaching the systemic circulation." The distribution of lead in the tissues will, therefore, vary with the route of absorption.

On being absorbed lead is probably transported in the blood stream in the form of colloidal lead phosphate and deposited in the tissues and, especially, the bones, as tertiary phosphate.[3] This storage of the lead in the bones renders the lead harmless only so long as it remains therein. Ordinarily the lead is released from the bones gradually, so that no symptoms of poisoning may be evident. However, the stored lead is very sensitive to changes in the hydrogen concentration of the blood and tissues, especially to such as may be caused by lactic acid, so that we may find dangerous symptoms suddenly arising by the rapid release of lead from its store-house. The fact that some individuals are more susceptible than others to the action of lead and, also, that the same individual varies in susceptibility at different times may have some relation to the route of absorption and to the rate of storage of lead. Further, some individuals apparently develop a certain degree of immunity to the effects of lead absorption following a period of exposure, a fact which seems to be borne out by experiments upon animals.[1]

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[1] Jour. Amer. Med. Assoc., 1927, 89, 1105.

[2] Kehoe, Edgar, Thamann and Sanders, Jour. Amer. Med. Assoc., 1926, 87, 2081.

[3] *Lead Poisoning*, by Aub, Fairhall, Minot, and Reznikoff, Medicine Monographs, Vol. VII, 1926.

Elimination of lead is largely in the feces, to a less extent in the urine, and very little by the bile and skin. It has been shown that so long as there is a positive calcium balance and a normal pH of the blood, the lead remains stored in the bones, so that the excretion of lead may be reduced to a minimum under these conditions. However, when a condition of either acidosis or alkalosis obtains, lead is dissolved out of the bones, which may explain why a sudden appearance of symptoms of lead poisoning may occur in an individual, who had not been exposed to lead absorption for some time. The rate of elimination of lead is slow and irregular, but may suddenly show a marked increase due to the conditions above-mentioned influencing mobilization of the stored lead.

Symptoms.—The susceptibility of different individuals to lead may determine whether or not a definite exposure is to be followed by the symptoms of acute or chronic poisoning. As Shie[2] states, "Some workers will develop an acute attack after working only a few days, while others may work for months at the same employment without harm."

Acute Poisoning.—The symptoms following the ingestion of a large amount of such a soluble lead salt as the acetate are, for the most part, those related to the local irritant action of the poison. The patient may complain of the sweetish, metallic, astringent taste of the solution as soon as the material is taken into the mouth. In a short time, usually within a half hour, more or less persistent vomiting will occur, associated with a colic-like paroxysmal abdominal pain, which is somewhat relieved be pressure. There may be purging, with bloody, dark-colored stools, although there is a tendency to constipation. There may be headache, pain and cramps in the legs, insomnia, great depression, coma and death.

In the acute types, which follow exposure to lead dust, and in the sudden exacerbations of the really chronic types of poisoning, there may be only mild symptoms of gastro-intestinal irritation, although as a rule the abdominal colic will be observed. This may develop suddenly or be preceded by a period of vague abdominal distress. In such cases the nervous symptoms appear to be especially prominent, the ordinary acute cases occurring relatively soon after exposure to the lead. In this form an acute neuritis may appear and, occasionally, a sudden paralysis may develop with almost no previous symptoms.[1] In other cases, which are more severe, the acute poisoning may manifest itself in the form known as lead encephalopathy, which is characterized by headache, epileptiform convulsions, delirium, maniacal excitement with or without delusions, partial or total blindness, paralysis, coma and death, although some cases recover or pass into permanent insanity.

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[1] See Weller, Arch. Int. Med., 1927, **39**, 45; Kehoe and Thamann, Amer. Jour. Pub. Health, 1928, **18**, 555.

[2] Jour. Amer. Med. Assoc., 1924, **83**, 580.

In these acute cases there may be such destruction of red blood cells that an acute anemia associated with the appearance of hematoporphyrin in the urine may be observed. There may even be a lead line along the borders of the gums and the red cells may show some basophilic strippling, although the acute types of poisoning which follow ingestion of large amounts of lead salts are ordinarily too rapid to permit of the development of these signs, which are more characteristic of the chronic types, or of acute exacerbations in those exposed to lead for some time.[2]

In cases of acute poisoning with tetra-ethyl lead, the following symptoms were noted by Thompson and Schoenleber in the five fatal cases occurring at Rahway, N. J.: The first symptom noticed is a marked fall in blood pressure, an accompanying fall in body temperature and a low pulse rate. Then symptoms of profound cerebral involvement appear, persistent insomnia, extraordinary restlessness and talkativeness, and delusions. The gait is like that of a drunken man, but there are no paralyses or convulsions. Finally, after a period of exaggerated movements of all the muscles of the body, with sweating, the patient becomes violently maniacal, shouting, leaping from the bed, smashing furniture, and acting as if in delirium tremens. The patient may finally die in exhaustion. There is no cyanosis or dyspnea; there may be vertigo, and the acute outbreak may be preceded by a period of anorexia, vomiting and diarrhea. Changes in the red blood corpuscles are marked. A lead line may be noted on the gums.[3] Gastric and intestinal cramps are not an important item in the clinical picture. "The lead is excreted in larger quantities than is seen in most cases of lead poisoning. Excretion occurs by way both of the kidneys and of the alimentary tract. Usually the excretion in the feces exceeds that in the urine for a corresponding period of time."[4]

Chronic Poisoning.—Evidence of absorption of lead is shown by the presence of lead in the urine and feces and, also, by the appearance of a lead line on the gums. It is undoubtedly true that these signs of absorption of lead may be detected, at least in many cases, before any symptoms of true poisoning are present, so that these signs should not be taken as evidence that damage to the organism has been done. "For certain diagnosis of early chronic poisoning, it is usually essential that at least one typical sign of *absorption* be present, and also two distinct signs of *generalized intoxication* by lead. There are four signs which most frequently appear during the early stage of the disease: (*a*) the ashen color of the skin, (*b*) the lead line on the gums, (*c*) stippling of the red blood cells, and (*d*) a mild secondary anemia or such other evidence of rapid peripheral destruction of blood as an increased quantity of blood pigment in the plasma or of hematoporphyrin in the urine."[1]

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[1] See Foshay, Jour. Amer. Med. Assoc., 1926, **86**, 1688, who reports a case of lead poisoning with onset simulating trigeminal neuralgia.

[2] Ockerblad, Jour. Urol., 1923, **10**, 271; McCord, Minster and Rehm, Jour. Amer. Med. Assoc., 1924, **82**, 1759; Shie, Ibid., 1924, **83**, 580.

[3] See Eldridge, Chemical Warfare Service, Report 29, 1924; Hamilton, Reznikoff and Burnham, Jour. Amer. Med. Assoc., 1925, **84**, 1481.

[4] Kehoe, Jour. Amer. Med. Assoc., 1925, **85**, 108.

It is probable that the most constant of these early signs is the ashen color of the face and the pallor of the lips, which is possibly due to the action of lead on the skin capillaries[2] as well as to the associated anemia. The most easily detected sign of lead absorption is the lead or Burtonian line on the gums. It is caused by a deposit of fine granules of lead sulphide in the deeper layers of the gums about 1 mm. from the border of the teeth. "Typically it appears around infected or pyorrheic teeth, but occasionally may be found in the buccal surfaces of the mucous membrane, i.e., on the inside of the lips or cheeks near decaying teeth." While copper, bismuth and silver may, possibly, cause a somewhat similar pigmentation, yet as a rule such a line is almost positive evidence that lead has been absorbed into the blood stream. It must be admitted that there are many cases of lead poisoning in which this lead line may not be evident, but in many of such subjects lead may be detected in the urine as an evidence of lead absorption. The presence of lead in the feces does not, in itself, prove that lead has been absorbed and later excreted, as all of the lead in this situation may have been insoluble and hence have been inert. This lead line may appear after slight exposures to lead and it may persist for some time after exposure has ceased.

One of the early signs of lead poisoning is a constant and mild secondary anemia, with a reduction in the number of red cells rarely below 3 million per cubic millimeter and a corresponding diminution in the percentage of hemoglobin. There may be some anisocytosis and some polychromatophilia, but the most characteristic change in the blood is the *basophilic stippling of the red cells*. While normal blood may show a few stippled cells and these may be present in increased numbers in benzene poisoning, arsenic poisoning, pernicious anemia, hemolytic jaundice, leukemia, polycythemia, and in malignant toxemia, yet they are present in larger numbers in those exposed to lead hazards, so that a count of 200 to 250 stippled cells per million erythrocytes may be taken as a criterion of danger to the exposed worker. McCord[3] has shown that in normal persons these stippled cells ordinarily number less than 1000 and never exceeded 5000 per cubic millimeter, but that in frank lead poisoning the counts almost invariably ran over 7000 and rarely over 100,000, the usual counts falling between 7000, and 50,000 although signs and symptoms of clinical lead poisoning may not appear even when the basophilic cell count is as high as 60,000 or 80,000. McCord believes that, when the count exceeds 6000 to 7000 per cubic millimeter and when other etiologic factors are absent, the worker should be considered a lead poisoning prospect. The stippling is characterized by the appearance, in the body of the red cells, of granules of varying size either evenly distributed throughout the cell or being grouped more thickly around the edges of the cell. These granules are in sharp focus with the edges of the red cells. These granules may vary in number from day to day and may appear very early in cases of lead poisoning and may be present in the blood for some time after exposure to the lead hazards. While these granules may be readily stained by Wright's stain by limiting the decolorization of the smear to the blue rather than the pink stage, yet Harrison's modification of Süssmann-Weindel's stain[1] seems to afford somewhat clearer pictures. It has been reported[2] that, at least in animal experiments, the number of poikilocytes and stippled cells ran parallel. Evidence of regeneration of blood cells may be shown in an increase in the number of reticulated cells, while peripheral destruction of the red cells may become evident by an increase of blood pigment in the plasma, pleiochromia of the bile, and the excretion of urobilin and hematoporphyrin in the urine.[3] Associated with this condition of rapid destruction of red blood cells, we may observe a slight jaundice.[4]

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[1] See *Lead Poisoning*, by Aub, Fairhall, Minot and Reznikoff, Medicine Monographs, 1926, **7**, 197. Also, Hirschhorn and Robitschek, Ztschr. f. klin. Med., 1927, **106**, 664.

[2] See Koelsch, Jahresk, f. ärztl. Fortbild., 1919, **10**, 15.

[3] "A New Test for Industrial Lead Poisoning," Bull. 460, Bureau of Labor Statistics, U. S. Department of Labor, April, 1928.

Along with the above signs, which are especially characteristic of absorption of lead, there may be a number of general symptoms, such as metallic taste in the mouth, anorexia, foul breath (halitosis), headache, nausea and vomiting, constipation, general weakness and a feeling of lassitude.

The above signs and symptoms may continue for some time with no marked increase in severity providing excretion is keeping pace with absorption, but sooner or later, in most cases at least, following an acute infection, excessive use of alcohol, or the presence of conditions inducing acidosis, excessive amounts of lead may be mobilized from their storehouse in the bones and acute manifestations, the so-called toxic episodes, will appear. These are colic, which is usually abdominal although any of the smooth muscles of the body may be affected; local paralyses, especially paralysis of the extensor muscles of the forearm leading to wristdrop, although the site of the lead palsy will depend upon what nerves and muscles are most used by the particular individual; encephalopathy, which has been previously mentioned; optic neuritis; and arthralgias. As late manifestations of the lead intoxication, we find generalized arteriosclerosis and chronic nephritis. As Pejic has shown, the earliest kidney lesions noted in animals are moderate parenchymatous and fatty degeneration, while after the poisoning has continued for about six months interstitial renal fibrosis begins and, later, the contracted kidney results.[1]

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[1] See U. S. Public Health Service, Bull. 163, 1926. Also, Leake, Jour. Amer. Med. Assoc., 1927, **89**, 1105. This stain is made as follows: Dissolve 0.5 gram of borax in 1 liter of distilled water, heating if necessary. To this add 5 grams of toluidin blue and 50 cc. of Loeffler's methylene blue. Filter and add 7.5 cc. of a 1 per cent aqueous solution of yellowish eosin just before using. Fix the blood smears in 96 per cent alcohol and stain 20 minutes in this solution. Wash and dry in the usual manner.

[2] Lehmann, Weindel, Jobs and Argus, Arch. f. Hyg., 1924, **94**, 38.

[3] See Teleky, Schrift. a. d. Gesamtgebiet d. Gewerbehyg., 1919, **5**, 1; Hirschorn and Robitschek, Ztschr. f. klin. Med., 1927, **106**, 664.

[4] See Lewin, Deutsch. med. Wchnschr., 1928, **54**, 1450.

Fatal Dose and Fatal Period.—The fatal dose of such soluble salts as lead acetate is probably somewhat greater than 25 grams, as recovery has occurred in at least 3 reported cases from doses of approximately 30 grams. However, much would depend upon the rapidity of absorption and the susceptibility of the individual. While death from acute poisoning is relatively rare, yet death has occurred from collapse as early as the second or third day.

Treatment.—Probably the type and severity of lead poisoning are determined more by the susceptibility than by the amount of lead absorbed. However the lines of treatment should be directed toward elimination and storage of the lead in the tissues, especially in the bones. In acute cases, the stomach should be washed out with a solution of magnesium or sodium sulphate, followed by plain water to remove the lead sulphate formed, as this latter compound is somewhat soluble in the gastric juice and would, therefore, be capable of absorption unless removed. The bowels may be evacuated by magnesium sulphate and washed out with high enemas. To control the abdominal colic hypodermic injection of morphine and atropine may be efficacious, although in some cases little effect is observed. As it has been shown by Aub and his associates that the amount of lead excreted has a definite relation to the calcium metabolism and that a positive calcium balance favors storage of lead while a negative balance tends to increase the rate of excretion, calcium should be administered in the form of milk and calcium lactate until the acute attack has subsided, probably as much as 1 quart of milk and 2 grams of calcium lactate per day being sufficient. It is probably true that during acute attacks no medication should be given which is directed toward mobilization of the stored lead, beyond seeing to it that elimination through the bowels and kidneys is kept up.

Following the suggestion of Ravaut[2], several workers such as McBride and Dennie[3], Ockerblad[4], Hoffmann and Schreus[5], Kuhn and Reese[6]

[1] Ann. Internal Med., 1928, **1,** 577.

[2] Presse méd., 1920, 28, 73.

[3] Arch. Dermat. & Syph., 1923, **7,** 63; Jour. Amer. Med. Assoc., 1924, **83,** 2082.

[4] Jour. Urology, 1923, **10,** 271.

[5] Münch. med. Wchnschr., 1923, **70,** 1481.

[6] Jour. Amer. Med. Assoc., 1925, **85,** 1804. See, also, Curtis and Young, Jour. Lab. & Clin. Med., 1928, **13,** 628.

have advised the intravenous injection of sodium thiosulphate, combined with lavage of the stomach with water containing this salt and the administration of it by mouth. The thiosulphate is given intravenously in not more than 20 cc. of distilled water for each dose, every day for 4 days and then every other day for as many doses as are necessary to produce the desired results, the beginning dose being 0.3 gram, the second 0.45 gram, the third 0.6 gram, the fourth 0.9 gram, the fifth 1.2 grams, the sixth 1.8 grams. This treatment will undoubtedly result in diminution of the ionized lead in the body fluids, but it will not prevent additional lead entering the blood from its store-house in the bones. The results with this treatment have been more or less satisfactory in arsenic and mercury poisoning, but its status in lead poisoning remains to be determined by future study.

In the chronic cases, the worker should be removed from contact with the lead hazard and attempts made to increase the elimination of any lead that may be stored in the system. Also, in cases in which there have been acute exacerbations, the same line of treatment should be followed as soon as the acute symptoms have subsided. Probably the most frequently used agent for this purpose has been potassium iodide, administered 3 times daily in doses increasing from 3 to 5 grains up to the limit of tolerance. While this medication does unquestionably increase the output of lead, for the most part in the feces, yet it must be remembered that potassium iodide may, not infrequently, precipitate an acute attack of lead poisoning in "leaded" individuals long after exposure to the lead hazard has ceased.

In line with the newer ideas relative to lead excretion and storage, the "deleading" is accomplished by maintaining a negative calcium balance and changing the hydrogen ion concentration of the blood by administering acids or acid-forming salts along with a diet containing little calcium, or by giving alkalies (sodium bicarbonate) alone. Either phosphoric acid, in doses of 20 cc. of the dilute phosphoric acid of the Pharmacopoeia (10 per cent.) in a glass of water about 10 times daily for several weeks, preferably ammonium chloride, in doses of 1 gram in a glassful of water 10 times daily may be used. If the alkaline treatment is preferred, 20 to 40 grams of sodium bicarbonate should be given daily. The administration of the salts of the light metals, such as sodium and potassium, tends to change the phase of the ion-protein compounds present in heavy metal poisoning, as shown by Fischer. In this treatment, the medication should be discontinued, when signs of acidosis or alkalosis appear. Recently Hunter and Aub[1] have found that the administration of parathyroid extract-Collip, in doses of 20 to 65 units daily, increases the excretion of lead. However, the effect is not continuous. Thus, when first given, the parathyroid extract markedly enhanced the lead output, but, if the lead output was large after the first administration, succeeding doses produced but little effect. These workers believe that this treatment "mobilizes from the bones a certain amount of stored lead which is readily available. The remaining lead is mobilized much more slowly in the usual routine of metabolism."

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[1] Quart. Jour. Med., 1927, 20, 123.

Postmortem Appearances.—In the acute cases the changes reported have not been especially characteristic. The mucous membrane of the stomach may show signs of a slight gastritis, while that of the bowel may be normal although colored somewhat black from the formation of lead sulphide. If the case has continued until general systemic disturbances arise, the liver may show cloudy swelling and the kidney evidences of a nephritis, tending toward the interstitial type.

In the autopsies reported upon 4 cases of acute fatal poisoning with tetra-ethyl lead[1] the chief findings were hemorrhagic bronchopneumonia and intense pulmonary engorgement, and in one of the cases there was a yellowish discoloration of the cerebral cortex and chronic leptomeningitis. All of the cases showed yellowish discoloration of the skin and hemorrhagic foci in the bone-marrow.

In chronic cases, the principal changes observed are a generalized arteriosclerosis and a contracted kidney with the general changes resulting from such conditions.

Detection.—As we have already stated, the distribution of lead in the system will depend upon the route of absorption. If absorbed from the gastrointestinal tract, a large part of the lead will be found in the liver, while the other organs will contain relatively little. If absorption occurs through the respiratory tract, all of the tissues and, especially, the bones, adipose tissue, and muscles, will contain varying amounts of lead, while the kidneys and brain may show fairly large amounts. As excretion is largely by means of the feces and less by the urine, both of these excretory products should be examined in case a definite idea of absorption is desired. Lead is not infrequently found in both the feces and urine of persons who have not been exposed to industrial hazards, so that the detection of small amounts of lead therein has little toxicological value[2]. Millet[3] has shown that "In cancer patients who had received injections of a lead phosphate colloid and in cancer patients not treated with lead the excretion was about the same, averaging about 0.085 mg. of lead per liter. There is a definite normal excretion of lead in the urine."

In the routine examination of tissues for inorganic poisons, lead will be found, unless present in very large amounts, in the *hot* filtrate obtained after decomposing the organic matter with hydrochloric acid and potassium chlorate. Some of the lead, however, may remain behind on the filter in the form of the sulphate and very small amounts of the chloride, so that the filtrate alone will not yield quantitative results in all cases, although, as a rule, the loss is slight. This filtrate is treated with hydrogen sulphide, when the lead present will be precipitated. Allow the lead sulphide to settle out, filter, wash with water, and dissolve in warm dilute nitric acid. Filter from the separated sulphur and evaporate the filtrate to dryness. Dissolve the residue in water and test for the presence of lead with sulphuric acid, potassium iodide, or potassium chromate in the usual qualitative manner. In case the amount of lead is very small, recourse may be had to the microchemical detection in the form of the hexanitrite of potassium, copper, and lead, as originated by Behrens and Kley and modified by Fairhall[1].

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[1] Norris and Gettler, Jour. Amer. Med. Assoc., 1925, **85**, 818.

[2] Kehoe, Edgar, Thamann, and Sanders, Jour. Amer. Med. Assoc., 1926, **87**, 2081; Kehoe and Thamann, Ibid., 1929, **92**, 1418.

[3] Jour. Biol. Chem., 1929, **83**, 265.

Determination.—In the quantitative estimation of lead in the tissues, feces or urine, the lead is best determined by the chromate method in the following manner. A weighed amount of the finely hashed tissue or of the feces is placed in a Coors porcelain dish, dried in the hot-air oven for 10 to 12 hours and then ashed in an electric or gas muffle at dull red heat. Fecal matter usually ashes readily but the tissues form a residue which must be repeatedly extracted before the entire char is consumed. After the first ashing the material should be cooled and extracted with dilute hydrochloric acid and hot water. It is essential that at this stage all the ash be dissolved. Filter, wash the residue with hot 10 per cent. HCl and then with hot water. Transfer the filter paper and residue to the original porcelain dish and ash again. This second ash is moistened with 10 cc. of water and treated with 5 cc. of 10 per cent. tartaric acid in 1:1 HCl and warmed. Filter and add this filtrate to the first one. Should the ash not be completely dissolved, treat again in the same manner. The combined filtrates are diluted with distilled water and neutralized with 25 per cent. NaOH solution until yellow to methyl orange. Adjust the reaction with HCl until the solution is just acid (pink) to methyl orange. Now saturate the cold solution with washed hydrogen sulphide, passing the gas for one hour. Cap the flask and allow the sulphide to settle over night. Filter and wash the precipitate with freshly prepared hydrogen sulphide water containing 0.1 per cent. HCl. Dissolve the washed precipitate in dilute nitric acid, boil to expel hydrogen sulphide and filter to remove the sulphur which separates. Cool and neutralize with NaOH solution, using phenolphthalein as indicator. Now acidify this solution with acetic acid and add 1 cc. of a 1 per cent. solution of potassium chromate, allowing the flask to stand in a warm place over night. Collect the precipitated chromate on a filter paper, washing thoroughly with hot water. Dissolve the precipitate on the paper with 10 cc. of cold 1:2 HCl followed immediately by cold water to the extent of about 50 cc. To this solution add an excess of potassium iodide solution (2 cc. of a 1 per cent. solution will usually suffice in the case of feces, but with tissues more may be necessary), and 1 cc. of 0.5 per cent. starch solution. Titrate the liberated iodine with a 0.005 N solution of sodium thiosulphate solution freshly prepared from a standardized 0.1 N solution. 1 cc. of 0.005 N sodium thiosulphate is equivalent to 0.3452 mg. of metallic lead.

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[1] Jour. Biol. Chem., 1923, 57, 455.

Lead in Urine.—Urine does not ash readily owing to the large quantity of inorganic salts present. For this reason the method of Fairhall[1] is especially valuable. This procedure is as follows: To as large a measured volume of urine as is at hand add ammonium hydroxide until the reaction is strongly alkaline. Allow the mixture to stand over night. In this reaction the earthy phosphates are precipitated and lead phosphate is carried down quantitatively by entrainment. The gelatinous mass of phosphates settles into a compact mass from which the clear lead-free liquor may be decanted and the remainder rapidly filtered by suction on a Büchner funnel. The filter paper containing the precipitate is then ashed as above described and the lead determined by the chromate method just discussed.

MERCURY

Mercury exists in nature partly in the form of the metal itself but, especially, in the form of the sulphide (cinnabar or vermilion). As is well known, mercury forms two series of compounds, the mercurous, which are relatively insoluble, and the mercuric, which are much more soluble and much more active. All of the compounds of mercury, as well as the metal itself, are poisonous providing, of course, that they are absorbed.

In recent years the medicinal use of mercury compounds has greatly increased, many new germicidal agents being introduced and many new anti-syphilitic combinations being advocated. The more modern method of employment of many of these mercurials by intramuscular or intravenous injection, instead of the older oral or dermic routes, may, possibly, lead to more toxic action, in some cases at least, but, nevertheless, the real toxicologic cases still follow the administration of the mercurial by mouth, or the absorption of these agents by mucous surfaces which have been brought in contact with solutions of mercury.[2]

The number of preparations of mercury and of mercury compounds used in medicine is large, and practically all of these have been accountable for some cases of death. Besides mercury itself, we find as official preparations of the metal the following: *Hydrargyrum cum creta* (mercury with chalk, gray powder), *massa hydrargyri* (blue mass, blue pill), *unguentum hydrargyri fortius* and *unguentum hydrargyri mite* (blue ointment). Official salts of mercury are *hydrargyrum ammoniatum* (white precipitate, mercurammonium chloride), *hydrargyri chloridum corrosivum* (corrosive sublimate), *hydrargyri chloridum mite* (calomel), *hydrargyri iodidum flavum* (yellow mercurous iodide, mercury protiodide), *hydrargyri iodidum* rubrum (red mercuric iodide, mercury biniodide), *hydrargyri oxidum*

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[1] Jour. Biol. Chem., 1924, **60**, 485.

[2] See Stock, Med. Klinik, 1928, **24**, 1154, for a discussion of the dangers of mercury poisoning from amalgam dental fillings. Also, Hertz, Klin. Wchnschr., 1929, **8**, 541.

flavum (yellow mercuric oxide), and *hydrargyri salicylas;* while official preparations of some of these salts are the *toxitabellae hydrargyri chloridi corrosivi* (corrosive sublimate tablets), *pilulae hydrargyri chloridi mitis compositae* (compound cathartic pills), *liquor arseni et hydrargyri iodidi* (Donovan's solution), *oleatum hydrargyri*, and *unguentum hydrargyri oxidi flavi.* Non-official compounds or salts are *oleum cinereum* (gray oil, a 30 per cent. combination of mercury with lanolin and olive oil), mercuric sulphide, mercuric sulphate, Turpeth mineral (basic mercuric sulphate), mercuric nitrate and mercuric cyanide; while in New and Nonofficial Remedies we find the following compounds, which have found more or less usage in the treatment of syphilis or as germicides: Flumerin, mercuric benzoate, mercuric oxycyanide, mercuric succinimide, mercurochrome-220 soluble, mercurol, mercurosal, mergal, meroxyl, metaphen, novasurol, and potassium mercuric iodide.

While pure mercury itself ordinarily produces little more than a slight stomatitis with salivation and, occasionally, diarrhea, yet it has proven fatal. Taylor[1] cites a case of a woman of 42 who swallowed two pounds of mercury at intervals, the mercury remaining in the body 9 days and the last portions being passed on the 14th day, the only apparent effect noted being slight salivation. Kockel[2] reports the recovery of 3477 grams (about 4¾ pounds) of mercury from the feces of an illegitimate child, no symptoms of poisoning resulting. Hedren[3] reports 4 cases of mercurial poisoning, one of which was fatal. The inhalation of mercury vapor is more dangerous than ingestion *per os*, as is shown by the case cited by Gadamer[4] of the death of a woman following inhalation of the vapor from 2.4 grams of mercury, which had fallen on a hot stove-lid: while the bursting of leathern bags on the ship Triumph liberated 3 tons of mercury and resulted in the illness of 200 men, two of whom died from the excessive salivation, and all of the animals on board died.[5] Müller[6] records a case of mercury intoxication arising from the copper amalgam fillings of the teeth.

Mercury with chalk is usually regarded as free from harmful effects, although the death of a girl of 5 in 8 days after taking 3 grains daily for 3 days is cited by Taylor, and Harper[7] reports the death of a boy of 11 in 4 days after taking 16 grains of the gray powder in a week. Blue mass has been reported as causing death in at least 4 cases, while blue ointment has proven fatal in 7 cases, and gray oil in at least 16 cases.[8]

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[1] *On Poisons*, 3rd Amer. Ed., 1875, p. 351.

[2] Arch. f. Kriminol, 1928, **83**, 308.

[3] Vrtljschr. f. ger. Med., 1905, 3F., **29**, Suplh., 57. See, also, Drügg, Deutsche med. Wchnschr., 1929, **55**, 1637.

[4] *Lehrbuch der chemischen Toxikologie*, 2te. Aufl., 1924, p. 202.

[5] Mentioned by Taylor, *On Poisons*, 3rd Amer. Ed., 1875, p. 352.

[6] Deutsche med. Wchnschr., 1929, **55**, 221. See, also, Hertz, Klin. Wchnschr., 1929, **8**, 541.

[7] Lancet, 1851, **2**, 1579.

[8] See Witthaus, *Toxicology*, 1911, p. 723.

All of the official salts of mercury have produced fatal results, some of them many and some few cases, but by far the most frequently employed mercurial is corrosive sublimate, which has been accountable for many hundreds of deaths. Thus, Witthaus[1] states that of 559 cases of bichloride poisoning mentioned in medical literature since 1800, 422 have been reported since 1879. Of these more recent 422 cases, 179 were caused by irrigation of the vagina or uterus or both with solutions of 1:1000 or of still higher dilution in obstetrical or gynecological cases, and of these 66 were fatal. Of 312 cases other than obstetrical and surgical, 132 were accidental, 126 suicidal, 15 by administration by quacks, 29 homicidal, and 10 of unknown origin. Lambert and Patterson,[2] writing in 1915, state that "Of the 155 cases of suicide by mercuric chloride recorded in the past twenty-five years, seventy-three, or nearly half of them, have occurred in the last two years." The Reports of the Chief Medical Examiner's Office of New York City for the years 1918–20 show 36 suicidal and 15 accidental deaths from corrosive sublimate, while in 1925 there were 10 suicidal and 14 accidental deaths, and in 1926, 14 suicidal and 7 accidental cases. In the reports of the Coroner's Office in Chicago one finds 25 suicidal and 17 accidental deaths in the years 1918–20. Gatewood and Byfield[3] state that from Jan. 1, 1920 to May 1, 1922 there were admitted to Cook County Hospital (Chicago) a total of 71 cases of mercuric chloride poisoning.

The use of the organic preparations of mercury in syphilis and as germicides is extensive and we find that fatal poisoning has occurred from many of these compounds. Thus, injection of the benzoate[4], of the salicylate[5], of the oxycyanide[6], and swabbing of an operative wound with meroxyl[7] have proven fatal. Johnstone and Keith[8] report that the toxicity of novasural is somewhat less than that of mercuric chloride when based on the amount of pure mercury contained and that the pathologic lesions produced in the kidney of the rabbit by toxic doses of novasurol (merbaphen) are identical with the lesions produced by other mercurials. One of the most widely used germicides is mercurochrome-220. The toxicity of this compound has been studied by several workers[9], who showed that 10 mgs. per kilo invariably killed rabbits in 24 hours, while dogs tolerated this amount very well. In the experimental work of Macht and Harden[1], the toxicity appeared to be somewhat less, the average lethal dose for rabbits being about 30 mg. per kilo of weight, the variation noted by them probably being due to the absence of certain impurities, which have been eliminated by improved processes in the manufacture of the drug. However, the possibility of fatal poisoning by this compound should be borne in mind, as St. George[2] has reported 5 cases of death, in which mercurochrome was used as a germicide, intense nephritis and marked lesions in the large intestine being found in each case and mercury being isolated from the viscera in "even larger amounts than were found in mercuric chloride poisonings."

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[1] *Loc. cit.*, p. 731. Witthaus gives an excellent bibliography of the cases of poisoning with salts of mercury up to 1911.

[2] Arch, Int. Med., 1915, **16**, 865.

[3] Ibid., 1923, **32**, 458.

[4] Gaucher, Jour. de mal. cutan., 1906, **18**, 282.

[5] Homberger, Ztschr. f. prakt. Aerzte, 1900, **9**, 9; Neubeck, Dermat. Ztschr., 1902, **9**, 470; Bartsch. Münch. med. Wchnschr., 1907, **54**, 2138.

[6] Thiroloix, Bull. med., 1907, **21**, 702. The famous Molineux case in New York (168 N. Y., 264) was a case of mercuric cyanide poisoning.

[7] Buckley, Jour. Amer. Med. Assoc., 1925, **84**, 1916.

[8] Arch. Int. Med., 1928, **42**, 188.

[9] See Young, White and Schwartz, Jour. Amer. Med. Assoc., 1919, **73**, 1483; Young, Surg. Gyn. & Obs., 1925, **40**, 97; Young, Hill and Scott, Arch. Surg., 1925, **10**, 813.

Mercurial poisoning has occurred from oral ingestion, from inhalation of mercury vapor, from absorption through the unbroken skin, from absorption from wounds and mucous surfaces, and from subcutaneous and intravenous injection[3], both acute and chronic cases arising depending upon the amount of intake, rate of excretion and method of introduction. Absorption of the soluble mercurials from the gastro-intestinal tract is very rapid, the mercury possibly circulating in the form of an albuminate or being taken up by the leucocytes, while the more insoluble compounds are absorbed much more slowly. Burmeister and McNally[4] have shown that the introduction, in the form of a slightly acid aqueous solution, of 0.024 gram of corrosive sublimate per kilo of dog is followed by its appearance in the blood within 10 minutes, while the mercury can be detected in the blood in 3 minutes following a dosage of 0.5 gram per kilo., degenerative changes leading to individual cell death taking place rapidly in the kidney and liver. In a series of experiments upon rabbits, Menten[5] found that the intravenous injection of as small amounts as 0.00002 gram of bichloride per kilo of weight causes microscopic pathologic changes in the rabbit's kidneys and liver, which changes are evident within 5 minutes after injection, while gross pathologic lesions could be detected in a short time subsequent to the injection of 0.005 gram per kilo, this latter figure agreeing closely with the lethal dose of corrosive sublimate of 0.004 gram per kilo as found by Barbour[6] and by Sansum[7], while Trusler, Fisher and Richardson[8] show that this intravenous dose uniformly kills in about 3 days and 2 and 3 mg. per kilo are fatal after intervals varying from 6 days to 6 weeks. Haskell, Carder and Coffindaffer[9] have determined the lethal dose *per os* for dogs to be 20 mg. of corrosive sublimate per kilo of body weight, while Zeigler[1] believes that the minimum lethal oral or intravenous dose of bichloride for the dog cannot be based upon the weight of the animal and that the lethal oral dose for the dog is 200 mg. and the minimum lethal intravenous dose for the dog is 40 mg.

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[1] Jour. Pharm. and Exp. Therap., 1928, **32,** 321.

[2] Jour. Amer. Med. Assoc., 1925, **85,** 2005.

[3] Harmon, Amer. Jour. Path., 1928, **4,** 321, reports 4 fatal cases following intravenous injection of between 5 and 6 grains of mercuric chloride (at least 6 mg. per kilo).

[4] Jour. Med. Res., 1917, **36,** 87.

[5] Jour. Med. Res., 1922, **43,** 315.

[6] Jour. Amer. Med. Assoc., 1915, **64,** 736.

[7] Ibid., 1918, **70,** 825. See, also, Goldblatt, Jour. Lab. & Clin. Med., 1928, **14,** 145.

[8] Arch. Int. Med., 1928, **41,** 234.

[9] Jour. Amer. Med. Assoc., 1923, **81,** 448.

Besides the acute mercurial poisoning above mentioned, there is a chronic form which is found among workers, who are brought into contact with mercury in various industrial pursuits, and is the result of inhalation of the vapor or of absorption through the skin. Such poisoning has been observed among the cinnabar mining operatives in Spain, Austria, Peru, China and in the Ural mountains, while there has been little investigation of its occurrence among our own miners in California. Metallic mercury finds rather wide use in the industries, in the making of mirrors, thermometers, barometers, vacuum pumps, incandescent lights, and *x*-ray machines. Mercury is used in making fulminate in munition plants, in fire gilding, and in soldering dry batteries. In the form of an amalgam it finds rather extensive use by dentists, Schulte[2] being able to find mercury in the urine of 10 dentists studied by him. In the process known as carroting in the making of felt hats, the acid nitrate of mercury is widely used. The number of cases of industrial mercury poisoning seems to be especially great among hatters' furriers and others in the hatters' trade. Thus Martial[3] found 60 per cent. of 250 hatters' furriers suffering from mercurialism, while Gilbert found evidence of mercurialism in 43.6 to 66.67 per cent. of those engaged in the various processes of fur preparation, Bates discovered in New York City 80 cases of chronic mercurial poisoning acquired in the hatters' trade, and Harris found 28 per cent. of 350 furriers and hat makers suffering from some form of mercurialism.[4] Further, some cases have arisen from the incautious use of mercurials in medical practice and from the use of mercurial cosmetics.

Symptoms.—The symptoms of mercurial poisoning will vary in rapidity of appearance and in type according to the method of administering the drug and upon the amount of the mercurial absorbed, of special importance in this connection being the solubility of the compound taken, the mercuric salts being more soluble and more active than the mercurous. No matter what the method of entrance of the mercury, it is excreted by the stomach and intestines as well as by the kidneys and, to a less extent, by the saliva, so that we may expect that some reabsorption of the mercury from the gastro-intestinal tract will occur and, in consequence, that the systemic action will be prolonged and that elimination of all the mercury from the system will require some time, that portion of the mercury combined in the tissues probably not being eliminated for several weeks.

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[1] Jour. Lab. and Clin. Med., 1925, **10**, 259.

[2] Arch. f. Hyg., 1914, **83**, 43.

[3] Rev. d'Hyg., 1911, **33**, 224.

[4] See Hamilton, "Industrial Toxicology" in *Legal Medicine and Toxicology* by Peterson and Haines, 1923, **2**, 781.

Acute Poisoning.—When taken by the mouth the symptoms appear almost at once, while if absorbed from the skin or from the mucous surfaces the signs of intoxication appear somewhat more slowly. There is an acid, metallic taste, constriction of the throat and a burning sensation in the throat and esophagus, these symptoms being more marked if the mercurial is in solution than if in solid form. The mucous membrane of the mouth and throat will be shriveled and show a white coating, and the irritation may be so marked that acute edema of the glottis may occur. Within a few minutes, ordinarily less than 5 and rarely as long as 30, severe symptoms arising from the gastro-intestinal tract will appear, although such symptoms may be delayed in very rare cases for longer periods, as in one case reported by Wood[1] of a delay of 1½ hours, while apparently Gatewood and Byfield[2] record a case in which vomiting did not occur for 4 hours after the ingestion of approximately 20 grains of the bichloride. Of course, with the less soluble mercurials the time elapsing before appearance of the symptoms will ordinarily vary from ½ to 2 or more hours. Marked pain in the stomach occurs and, associated with it, there is violent, almost continuous vomiting of mucoid material frequently containing blood and shreds of mucus membrane. Soon there follow abdominal pain and severe purging of liquid, bloody stools, associated with considerable tenesmus and rectal pain. The pulse is small, thready and irregular; the respiration is labored; the urine may be scanty or suppressed from the start, although as a rule the total anuria is of gradual development; collapse associated with coma or convulsions follow; and death may ensue from the severity of the gastro-enteritis. Goldblatt[3] calls attention to the early progressive leukocytosis, the white count showing a rapid drop to normal during the period of convalescence. The above is the usual sequence of events in the more rapidly fatal cases, in which the symptoms are related almost entirely to the alimentary canal.

In many cases of acute mercurial poisoning salivation appears within two or three days, although it is not always seen, while in some cases it may appear within the first two hours of the poisoning. Associated with this salivation, there may be glossitis, gingivitis with loosening of the teeth, the buccal structures may be enormously swollen, and edema of the glottis may be sufficiently extensive to produce asphyxia.

In regard to the suppression of the urine it is to be said that anuria may be observed very early in some cases, while, in others, its appearance may be delayed for days. If absorption of the mercury is rapid, early kidney involvement will appear, so that we may expect signs and symptoms of the renal irritation to be shown soon or late, depending upon the amount of the mercury which is absorbed. The work of MacNider[1] would seem to indicate that the diminution of the urine in experimental cases with severe enteritis is "probably dependent upon a disturbance in the functional capacity of the vascular mechanism of the kidney induced by the deflection of arterial blood away from the kidney to the splanchnic viscera", as the kidneys of these animals show no degenerative changes. He points out that the injury to the kidney, in cases which survive the enteritis, has been constantly associated with the development of an acid intoxication, the formation of urine rapidly decreasing as the intoxication progresses. In those clinical cases of rapid death in a few hours, apparently from circulatory collapse as a result of the severe enteritis, Kohn[2] suggests that direct myocardial damage may account in part, at least, for the early toxic death. In cases in which death occurs after several days, this is usually due to the acute tubular nephritis which has been set up.

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[1] Jour. Amer. Med. Assoc., 1915, **64**, 507. See, also, Goldblatt, Amer. Jour. Med. Sci., 1928, **176**, 645.

[2] Arch. Int. Med., 1923, **32**, 456.

[3] Amer. Jour. Med. Sci., 1928, **176**, 645.

In these acute mercurial cases the nitrogenous elements of the blood show more or less constant variation from the normal, in the sense that there is retention of non-protein nitrogen, consisting of urea, uric acid, creatinin, creatin, amino acids, and undertermined nitrogen.[3] It is probable, however, that one should be guarded in drawing prognostic conclusions from the relative increase in any of these factors. There is a reduction of the alkali reserve in these cases and a marked diminution of the blood chlorides (hypochloremia) may occur, which is probably due to loss of chlorides through the vomiting.[4]

Chronic Poisoning.—In chronic mercurial poisoning the symptoms are modified by the fact that the mercurial is taken into the system in small doses over a long period instead of in a single large dose, although, occasionally, a chronic type may follow an acute case. In consequence of this slow administration of the drug, the violent corrosive action is missing, but there is loss of appetite, nausea and vomiting, often colicky pains and diarrhea, along with more or less general depression. The urine usually contains demonstrable amounts of mercury and the differential blood count reveals an increase in the number of lymphocytes.[5] In a few days salivation usually occurs, attended with swelling and tenderness of the salivary glands, the gums become red, spongy and tender and, occasionally, a blue line is noticed along the borders of the gums, the tongue may become swollen, ulcers may form in the mouth, the breath

[1] Jour. Exper. Med., 1918, **27**, 519.

[2] Arch. Int. Med., 1926, **37**, 225.

[3] See Myers and Fine, Jour. Biol. Chem., 1915, **20**, 391; Underhill, New York. Med. Jour., 1915, **102**, 662; Myers and Lough, Arch. Int. Med., 1915, **16**, 536; Campbell, Ibid., 1917, **20**, 919; Gatewood and Byfield, Ibid., 1923, **32**, 456; Weiss, Ibid., 1924, **33**, 224; Looney, Jour. Biol. Chem., 1926, **70**, 513; Goldblatt, Amer. Jour. Med. Sci., 1928, **176**, 645.

[4] See Heim, Schweiz. med. Wchnschr., 1925, **55**, 1085; Trusler, Fisher and Richardson, Arch. Int. Med., 1928, **41**, 234.

[5] See Lüddicke, Klin. Wchnschr., 1928, **7**, 398.

is very fetid, and the teeth may be loosened and, in the more severe cases, an acute periostitis may occur. Later, following a period of depression, there may be loss of weight, anemia and a general cachexia, occasionally associated with various types of skin eruptions which vary markedly in intensity. Disturbances of the nervous system now appear, characterized by insomnia, loss of memory, loss of self-confidence, irritability and, occasionally great cerebral excitability. A peculiar tremor appears to be somewhat characteristic of the slower forms of poisoning. This tremor is first noticed in the tongue, lips and eyelids and spreads to the arms and legs. It is always an intention tremor, increased by observation and by efforts to control it, and has a tendency to progress but subsides when the individual is at rest. The muscles steadily grow weaker, but there is no atrophy and the electrocontractility remains intact. Along with these disturbances of the motor areas, disturbances of sensation are not uncommon, while in some cases affections of the sight and hearing may occur. In these chronic cases death may occur from exhaustion, from the severe stomatitis, and, especially, from the chronic nephritis which usually results from the changes brought about by the mercury.

Fatal Dose.—The smallest possible fatal dose of a mercurial is a difficult matter to state, owing to the fact that an indeterminate amount is usually lost during the severe vomiting and the actual quantity taken can rarely be determined accurately, so that the amount absorbed is never known. It is, of course, clear that the lethal dose varies with the different mercurials and with the method of administration, so that we can state only the figures given in reported cases, leaving the inference that the true fatal dose is probably less than the smallest quantity known to have actually caused death.

Kobert[1] gives as the lethal dose of corrosive sublimate 0.18 gram (2.78 grains), while Kunkel[2] estimates it at 0.1 gram (1.54 grains). If we apply the figures of Trusler, Fisher and Richardson[3] of 2 and 3 mg. per kilo as the fatal dose for rabbits to an adult weighing 150 pounds, we find that between 2 and 3 grains would represent the probable minimum fatal oral dose. Taylor[4] cites a case in which there is reason to believe that 2, or not more than 3 grains, proved fatal to an adult; and a second case in which 5 grains, taken dissolved, produced death in 6 days. Rosenbaum[5] reports a fatal case in a child of 1¼ years following a dose of 0.06 gram (0.9 grain), while Taylor mentions a death of a child following the taking of 3 grains of bichloride, the dose being accurately determined from the fact that a prescription was made up by mistake for calomel. If the drug be given by intravenous route the fatal dose is smaller, as shown in the case reported by Lambert and Patterson[1] of the accidental intravenous injection of 1½ grains with death in 5½ days. It is probable that much smaller doses have produced death, when vaginal or intra-uterine irrigation has been used. Thus Vöhtz[2] used a quantity of a 1:750 solution (for irrigation after an abortion at 3 months) which contained about 0.25 gram (3¾ grains), the woman dying on the 10th day; while Braun[3] reports the death of a woman in 7 days after intra-uterine irrigation with a liter of a 1:3000 solution, the total quantity injected being 0.34 gram (5¼ grains). In such cases, only an indeterminate amount of the quantity injected could possibly be absorbed, so that much smaller amounts must have been fatal. While the above amounts of corrosive sublimate have caused death, recovery has resulted after administration of 6.5 grams (100 grains)[4] and, in a rather indefinite case, following a dose of 25 to 30 grams (386 to 463 grains).[5]

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[1] *Lehrbuch der Intoxikationen,* 2te. Aufl., 1906, **2,** 326.

[2] *Handbuch der Toxikologie,* 1899, p. 139.

[3] Arch. Int. Med., 1928, **41,** 234.

[4] *On Poisons,* 3rd Amer. Ed., 1875, p. 367. (*Reg. v. Robertshaw,* Carlisle Lent Assizes, 1845).

[5] Fortschr. der Med., 1921, p. 985.

Gray powder has proven fatal in a girl of 5 in 8 days after administration of 3 grains daily for 3 days[6]; while blue mass pills[6], given to a girl of nineteen in doses of 3 grains twice daily for 3 days (18 grains), have caused death in 12 days. White precipitate has proven fatal in doses of 20 grains in a child[7] and of 35 grains in an adult[8]; calomel has caused death in a boy of 14 in 3 weeks from the effects of 6 grains[9], while a woman has died from an oral dose of 0.9 gram (13.9 grains)[10] and another[11] following three hypodermic injections of 0.1 gram (1½ grains) each during a month, death following about 3 weeks after the last injection; mercuric iodide (biniodide) his proven fatal in 4 days from the effects of irrigation with a 1:2000 solution after normal delivery[12], while 25 grams (386 grains) *per os* caused death in 40 hours[13]; mercuric oxide has been responsible for suicide in a dose of about 30 grains dissolved in acetic acid[14]; and mercuric salicylate[15] has proven fatal in 57 days following the injection of 72 mg. (1.11 grains). Of the unofficial compounds the cyanide has caused death in doses of 0.65 gram (10 grains)[16], the oxycyanide in amounts of 0.02 gram (0.3 grain)[1], Turpeth mineral in a child in a dose of 3 grains[2] and in an adult in a dose of 2.6 grams (40 grains)[3], and the succinimide[4] in a dose of 0.2 gram (3 grains).

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[1] Arch. Int. Med., 1915, **16**, 865.

[2] Hosp. Tid., 1884, 3R., **2**, 557. Cited by Witthaus, *Toxicology*, 1911, p. 735.

[3] Wien. med. Wchnschr., 1886, **36**, 740.

[4] Lodge, Brit. Med. Jour., 1888, **2**, 720. See, also, Zamboni, Rif. Med., 1929, **45**, 327.

[5] Med. mod., 1904, **15**, 41.

[6] Taylor, *On Poisons*, 3rd Amer. Ed., 1875, p. 357.

[7] Short. Med. Times and Gaz., 1860, **1**, 444.

[8] Mann, *Forensic Medicine and Toxicology*, 1893, p. 448.

[9] London Med. Gaz., 1836, **18**, 484.

[10] Le Clerc, Ann. d'Hyg., 1902, 3 s., **47**, 379.

[11] Runeberg, Deutsch. med. Wchnschr., 1889, **15**, 4. See, also, Backer, Hospitalstid., 1921, **64**, 737; Burnett and Pestal, Colorado Med., 1924, **21**, 313 (death from 4 grains 19 days after ingestion of the calomel).

[12] Cited by Witthaus, *Toxicology*, 1911, p. 737.

[13] Grawitz and Waegner, Ztschr. f. klin. Med., 1927, **106**, 783.

[14] Nicholson, Brit. Med. Jour., 1896, **1**, 19.

[15] Neubeck, Dermat. Ztschr., 1902, **9**, 470.

[16] Thibert, Amer. Jour. Med. Sci., 1842, n. s. **3**, 490.

Fatal Period.—It has been stated[5] that death from corrosive sublimate has occurred in less than half an hour, while Hickenbotham[6] reports a death from mercuric nitrate in 25 minutes. Such cases must be regarded as very rare, as death occasionally occurs in from 3 to 5 hours[7], although life is ordinarily prolonged for 3 to 5 days or even longer and in some cases for 2 to 3 weeks. Calomel has proven fatal in 5 days[8] from a dose of 1 gram (15½ grains) in 2 days; mercuric oxide in 2 days after a dose of 1 ounce[9]; mercuric iodide in 40 hours[10]; while death has been delayed for 57 days following injection of the salicylate[11].

Treatment.—The treatment of mercuric poisoning is more or less uncertain, owing to the fact that it is very difficult to combat the effects once the renal lesions and the intestinal irritations have been well established. Although Sansum[12] is very pessimistic about any type of treatment, providing a minimum lethal dose is absorbed, yet cases of recovery from large doses have undoubtedly occurred. The principal indications would seem to be to prevent absorption of the mercury as far as possible, to hasten its elimination and to combat the acidosis, which seems to be associated with the development of the renal lesions as shown by MacNider. It is undoubtedly true that we have both recovery and death from toxic doses of mercuric chloride, that is that death does not necessarily follow the intake of a large amount of this poison. Further, the lines of treatment, which have proven effective with some workers, have been deemed worthless in the hands of others. It is evident that the success of any line of treatment will depend largely on the time elapsing, after the toxic intake, before the treatment is begun. If there is much delay, absorption of sufficient amounts of mercury to produce serious effects on the kidney may have already occurred, so that the measures taken to prevent absorption may not prove of much value. In cases, which have reached the stage of marked suppression of the urine, indicative of serious renal injury, favorable results from any line of treatment may be regarded as questionable.

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[1] Thiroloix, Bull. med., 1907, **21,** 702; Merkel, Vrtljschr. f. ger. Med., 1914, **47,** Sup., 193.

[2] Northrup, Proc. N. Y. Path. Soc., 1890, p. 35.

[3] Taylor, *On Poisons,* 3rd Amer. Ed., 1875, p. 386.

[4] Hofmann-Haberda, *Lehrbuch der gerichtlichen Medizin,* 11te. Aufl., 1927, p. 829.

[5] Taylor, *Loc. cit.,* p. 369.

[6] Brit. Med. Jour., 1872, **1,** 113.

[7] See Northrup (Proc .N. Y. Path. Soc., 1890, p. 35) for death of a child in 3 hours from 3 grains of turpeth mineral; Skegg (Lancet, 1863, **1,** 119) for the death of an adult in 3¼ hours from 112 grains of corrosive-sublimate; and Moore (Brit. Med. Jour., 1885, **2,** 15) for a death from 40 grains of white precipitate in 5 hours.

[8] Adam. Diss. Würzburg, 1892. Cited by Witthaus, *Toxicology,* 1911, p. 728.

[9] Sobernheim, *Handbuch der praktischen Toxikologie,* 1838, p. 250.

[10] Grawitz and Waegner, Ztschr. f. klin. Med., 1927, **106,** 783.

[11] Neubeck, Dermat. Ztschr., 1902, **9,** 470.

[12] Jour. Amer. Med. Assoc., 1918, **70,** 824.

As soon as possible administer protein in the form of several raw eggs beaten up in a quart of milk[1] and then evacuate the stomach with the tube or emetic if necessary. Gastric lavage may then be carried out, using 500 to 1000 cc. of a fresh solution of calcium sulphide[2], 1 grain to the ounce of water, in order to precipitate any mercury that may remain. This gastric lavage should be continued until the stomach washings are free from mercury, and should be repeated night and morning for some time to render insoluble any mercury that may have been reexcreted into the stomach. Zeigler[3] recommends that this treatment be followed by the introduction of 300 cc. of mucilage of acacia to prevent the corrosive action of the mercurial and to retard its absorption. Instead of using the calcium sulphide to precipitate the mercury in the stomach and bowels, one may employ the antidote of Carter[4], in the effort to render the mercury harmless by reducing it to the mercurous form. This antidote of Carter consists of 6 grains (0.4 gram) of sodium phosphite and 4 grains (0.25 gram) of sodium acetate; if this material be not at hand, use the antidote of Fantus[5], which is sodium hypophosphite 1 gram, water 10 cc. and hydrogen peroxide 5 cc., employing this every eight hours for two days until 10 times as much phosphite or hypophosphite has been given as of the suspected mercurial. Follow this with a copious lavage of the stomach with the above antidote diluted 20 times, until the mercury disappears from the washings. Rosenbloom[6] employs both the calcium sulphide and the phosphite or hypophosphite, following the former with the latter, but this would not seem to be necessary. Along with either line of antidotal treatment, it is wise to attempt to eliminate the mercury from the intestines and to render it harmless by colonic flushings with calcium sulphide solutions or the diluted antidotes of Carter or Fantus. Although some workers, especially Sansum[7], believe that efforts directed toward hastening the elimination of the mercury are fruitless, Lambert and Patterson[8] have obtained good results by this method. After the preliminary administration of eggs and milk followed by repeated lavage, these workers give, as soon as the irritability of the stomach will permit, 8 ounces of the following mixture every other hour: Potassium bitartrate, 1 dram; sugar, 1 dram; lactose, ½ ounce; lemon juice, 1 ounce; and boiled water, 16 ounces. This intake is alternated with 8 ounces of milk every other hour. Along with this treatment, they advise the continuous rectal irrigation with a solution of potassium acetate, a dram to the pint, and colonic irrigation twice daily; and daily sweats in a hot pack to assist the elimination. Weiss[1] advises the giving of alkaline waters or a solution of sodium bicarbonate in the lavage water and the intravenous injection of Fischer's solution[2] to combat the acidosis, the urine being kept alkaline, if possible, to methyl red. As further aids in the elimination of the mercury, Burmeister[3] advocates repeated venesection and transfusion, while Milian and Saint-Avid[4] recommend intravenous injection of alkali and glucose. Hayman and Priestley[5] insist on the importance of diuresis in the treatment of many of these cases and advise the intravenous injection of from 1650 to 2790 cc. daily of physiologic solution in addition to copious volumes of fluid by mouth.

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[1] See Sollmann, Barlow and Biskind, Jour. Amer. Med. Assoc., 1927, **88**, 623.

[2] See Hayward and Allen, Jour. Amer. Med. Assoc., 1913, **60**, 1827; Wilms, Jour. Lab. and Clin. Med., 1917, **2**, 445; Haskell and Courtney, Ibid., 1917, **3**, 110; Holm, Jour. Mich. State Med. Soc., 1917, **16**, 270; McCants, U. S. Naval Med. Bull., 1924, **20**, 572.

[3] Jour. Lab. and Clin. Med., 1925, **10**, 259.

[4] Chicago Med. Recorder, 1914, **36**, 444. This is a modification of Linhart's antidote (New York Med. Jour., 1913, **97**, 1236; Jour. Lab. and Clin. Med., 1917, **2**, 722).

[5] Jour. Lab. and Clin. Med., 1916, **1**, 879; Fantus and Hyatt, Ibid., 1917, **2**, 813.

[6] Amer. Jour. Med. Sci., 1919, **157**, 348 See, also, Gatewood and Byfield, Arch. Int. Med. 1923, **32**, 456.

[7] Jour. Amer. Med. Assoc., 1918, **70**, 824.

[8] Arch. Int. Med., 1915, **16**, 865. See, also, Lewis and Rivers, Johns Hopk. Hosp. Bull., 1916, **27**, 193; Cohen and Bernhard, Jour. Amer. Med. Assoc., 1916, **67**, 1019; Brown and Baskett, Ibid., 1917, **68**, 1622; Haskell, Carder and Coffindaffer, Ibid., 1923, **81**, 448.

McBride and Dennie[6] have advised the oral and intravenous administration of sodium thiosulphate according to the method outlined on page 449. While the results by this method have proven quite satisfactory in the hands of many workers, yet with others the treatment has proven of little avail. Like the other methods advocated, this treatment is uncertain in those cases in which the mercury has been absorbed.

In the chronic cases, improvement may follow removal of the patient from exposure to the mercury, but the elimination of all the mercury from the system is rather slow following repeated administration of small doses. Measures, such as those previously outlined, may be employed to increase the elimination, special attention being paid to the activity of the bowels and skin. Potassium iodide has been recommended for this purpose, but its efficacy is very doubtful, as has been shown by Souchow[7]. The general treatment should be symptomatic and efforts should be made to control the general weakness and anemia.

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[1] Jour. Amer. Med. Assoc., 1917, **68**, 1618; Arch. Int. Med., 1924, **33**, 224.

[2] This consists of 10 grams of crystallized sodium carbonate and 15 grams of sodium chloride dissolved in 1000 cc. of distilled water. If this is not available, a 4 per cent. solution of sodium bicarbonate may be used.

[3] Jour. Lab. and Clin. Med., 1917, **2**, 500. See also, Haskell, Carder, and Coffindaffer, Jour. Amer. Med. Assoc., 1923, **81**, 448; Haskell, Hamilton, and Henderson, Jour. Lab. and Clin. Med., 1926, **11**, 707.

[4] Paris méd., 1917, **7**, 213.

[5] Amer. Jour. Med. Sci., 1928, **176**, 510.

[6] Arch. Dermat. and Syph., 1923, **7**, 63. See, also, Sabbatani, Biochem. Centralbl., 1906, **5**, 502; Riforma med., 1907, **23**, 767; Ravaut, Presse méd., 1920, **28**, 73; Hoffmann and Schreus, Münch. med. Wchnschr., 1923, **70**, 1481; Dennis and McBride, Jour. Amer. Med. Assoc., 1924, **83**, 2082; Semon, Brit. Med. Jour., 1924, **1**, 662; Halliday and Sutherland, Ibid., 1925, **1**, 407; Fuss and Dahlman, Münch. med. Wchnschr., 1925, **72**, 345; Kuhn and Reese, Jour. Amer. Med. Assoc., 1925, **85**, 1804; Haskell, Henderson and Hamilton, Ibid., p. 1808; Cenini, Gazz. d. Osp. e. d. Clin., 1929, **50**, 373.

[7] Jour. de Pharm. et de Chimie, 1887, 6s., **15**, 367; Bull. gen. de therap., 1887, **112**, 133.

Postmortem Appearances.—If the mercurial has been taken by the mouth, some part of the alimentary tract will show inflammatory changes. In the rapidly fatal cases in which the bichloride or nitrate has been taken, the lips, tongue, buccal and pharyngeal mucous membranes may be swollen, covered with a grayish-white, or even black coating, and may be shriveled. Such local lesions may be almost entirely absent if the solution was taken well back into the throat before swallowing and will not appear with the non-corrosive mercury compounds. In the cases associated with salivation and stomatitis, there may be extensive ulceration and necrosis, the gums may be softened, the teeth loosened and the salivary glands may be extensively infiltrated. The esophagus and stomach show evidences of corrosion, this occasionally being sufficient to produce ulceration and even perforation. The duodenum may show similar signs of corrosion, but the remaining portions of the small intestines ordinarily shows nothing beyond slight congestion. The appearances of the large intestines are quite characteristic and resemble those associated with severe dysentery, the lesions being especially noted in the coecum and sigmoid flexure of the colon. These lesions in the large intestine appear to be present, to a more or less extent, in those cases in which the mercury has been *given by parenteral methods,* although gastric lesions do not seem to occur after intravenous injection of large doses of mercury according to Harmon[1].

The renal lesions are practically constant and characteristic. The toxic nephrosis is evident in a high-grade parenchymatous degeneration and edematous swelling of the kidney. The kidneys are large and soft, the cortex being pale and sharply outlined from the red medullary portion. Microscopically there is necrosis of the epithelium of the convoluted tubules and, occasionally, of the loops of Henle, while the necrotic epithelial cells, as well as the lumen of the tubules, show a deposition of calcium carbonate and phosphate, which may be very extensive or may, occasionally, not be present. In Harmon's[2] 4 cases of death from intravenous injection of mercuric chloride, the epithelial damage in the kidneys ranged from parenchymatous degeneration to necrosis with calcification, the renal changes being essentially the same as in cases in which the mercury is given by mouth.

The liver may show, especially in prolonged cases, some fatty degeneration, while there may be some degeneration of the cardiac muscle and ecchymoses of the endocardium and pericardium.

Detection.—In cases of mercury poisoning in which death is rapid, the stomach and small intestines usually show the largest amounts, while the liver and kidneys, also, contain appreciable quantities. In the cases in which mercury has been introduced parenterally, the largest proportion of the absorbed poison will, probably, be found in the kidneys or the liver, while the large intestine will usually contain more or less notable

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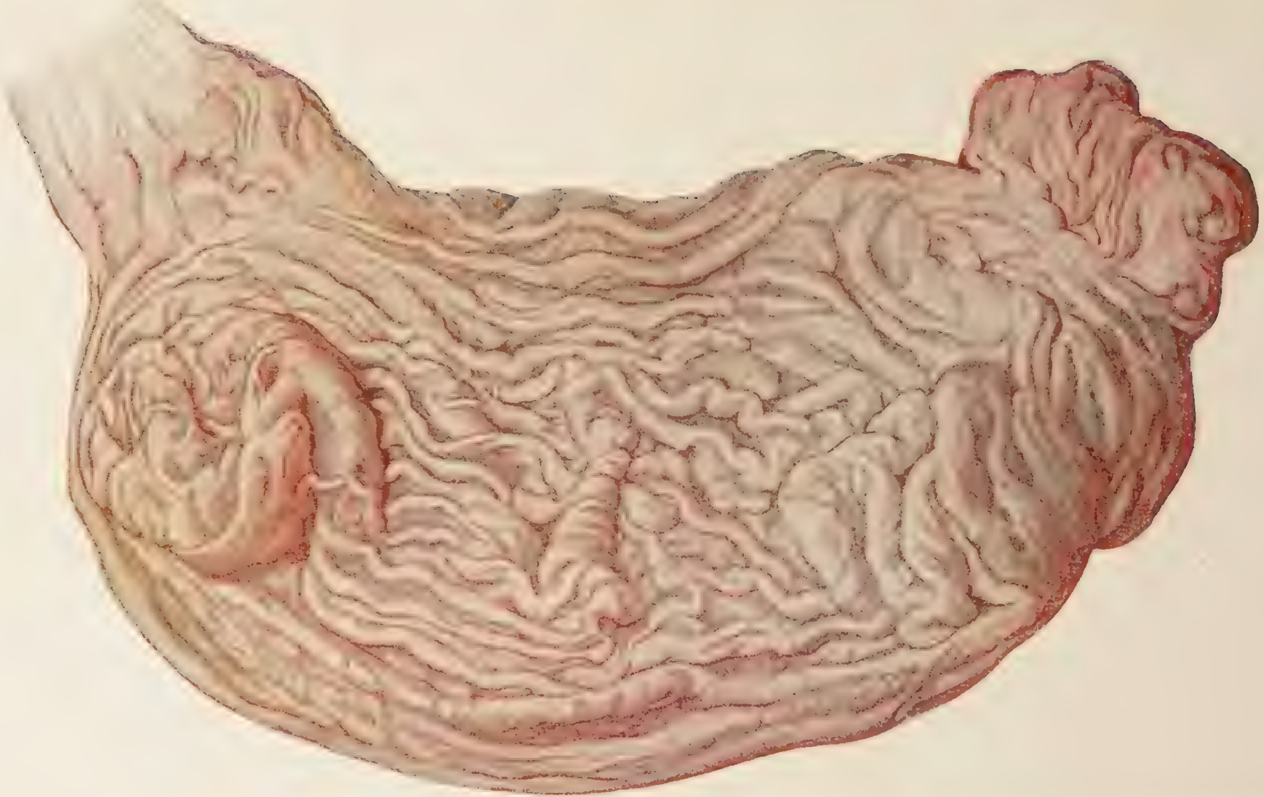
[1] Amer. Jour. Path., 1928, 4, 321.

[2] *Loc. cit.*

PLATE II



Stomach After Acute Poisoning with Corrosive Sublimate (Von Hofmann). A hospital nurse poisoned herself with a concentrated solution of corrosive sublimate, and died from collapse [illegible] persistent vomiting. A grayish white eschar was diffused over the mucous membrane of the lips, mouth, and pharynx. At the necropsy the same appearance was found in the esophagus and stomach. The stomach was firm and contracted, looking as if cooked. The entire mucous membrane and part of the submucosa were colored a uniform pale violet. The walls were thickened, and fell into coarse folds. The changes were those of "coagulation necrosis." The peculiar color is the result of the mouse-gray tint of the coagulated blood in the vessels, blending with the white escharotic tissue of the epithelium

amounts. The elimination of a single non-fatal dose of mercury may be practically complete in a few days, although occasionally some mercury may be eliminated for a week or more; after repeated small doses, the elimination is slower, so that one may not be surprised to find traces in the urine a month or so after discontinuance of the mercurial. Cases have been reported[1] in which death occurred in a short time and yet no mercury was detected, but this must be regarded as rather unusual. On account of certain possibilities of loss in the examinations, small amounts of mercury may, of course, escape detection, yet in the usual toxicological cases, such loss of mercury may almost be disregarded. Sartori[2] was unable to detect 1 mg. of corrosive sublimate added to organic matter and believes that the organic matter escapes complete destruction in the process of Fresenius and von Babo and prevents the typical reactions. However, much smaller quantities than 1 mg. have been detected by many workers in toxicological cases, so that some other factor must have played a role in the experiments of Sartori. A possible loss of mercury may arise from the reduction of the salts to metallic mercury by the organic matter, so that this amount may escape detection unless the original insoluble residue obtained in the process of decomposition be repeatedly submitted to the action of oxidizing agents. If the amount of mercury be small, one may find that the process of precipitation with hydrogen sulphide will result in the formation of more or less colloidal sulphide which is not filterable, but such small quantities rarely play a role in toxicological cases.

In the systematic examination of the tissues for metallic poisons, as discussed on page 341, mercury will ordinarily be found in the precipitate produced by hydrogen sulphide in the filtrate from the decomposition of the organic matter by hydrochloric acid and potassium chlorate, although the possibility of loss as mentioned above must be borne in mind. If the quantity of mercury be very small no precipitation may occur at this point, as the mercury may exist in the colloidal, non-ionized form, but such possibilities rarely interest the toxicologist. However, if the question of the presence of such small amounts seems important, recourse may be had to the method of Booth, Schreiber and Zwick[3], which is extremely accurate and delicate. On treatment of the mixed sulphides in the usual manner of qualitative chemical analysis, mercury will remain as a residue insoluble in hot dilute nitric acid. This insoluble mercuric sulphide may then be tested by the reduction and sublimation test, or it may be dissolved in *aqua regia*, evaporated to dryness at a low temperature, redissolved in warm water and the usual qualitative tests applied, such as the stannous chloride, potassium iodide, ammonium thioacetate, diphenylcarbazide, or amalgamation with copper tests, the details of which may be found elsewhere.

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[1] See Church, Edinb. Med. Jour., 1887, **32,** 795. In this case death occurred in 22 hours after intake of the toxic dose and yet no mercury was found in the organs examined.

[2] Chem. Ztg., 1924, **48,** 141.

[3] Jour. Amer. Chem. Soc., 1926, **48,** 1815. See, also, Booth and Schreiber, Ibid., 1925, **47,** 2625; and Schreiber, Sollmann and Booth, Ibid., 1928, **50,** 1620.

Amalgamation Test.—This test is one of the most delicate and most characteristic of the tests for mercury. It is especially serviceable in testing stomach contents, urine, feces, and tissues in general for mercury, as it may be performed without previous decomposition of organic matter and, hence, may be employed as a preliminary test for the presence of mercury. If no mercury be found by this test, especially when certain modifications are introduced, then one may be practically certain that mercury is not present in amounts which are of toxicological interest.

The test is based on the fact that metals, which are more electropositive than mercury (such as copper, zinc, iron and aluminum), liberate metallic mercury from solutions of both mercuric and mercurous salts. There are several methods of performing this test, of which the following have proven very satisfactory.

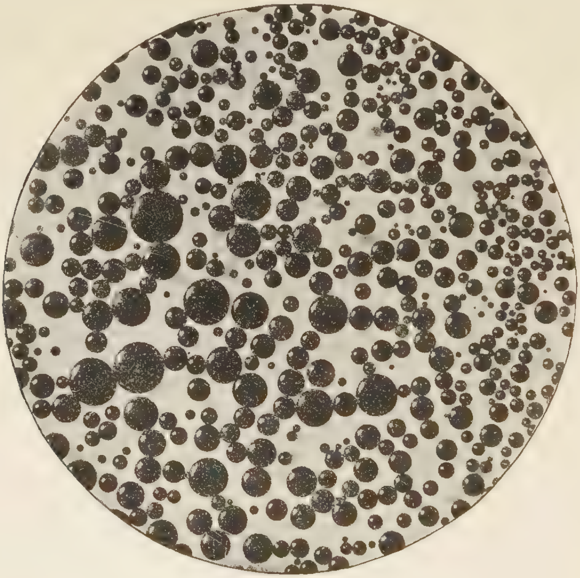

Fig. 40.—Sublimate of metallic mercury magnified. (Holland in Peterson, Haines and Webster, "Legal Medicine and Toxicology.")

Reinsch's Test.—Take a portion of the urine (preferably concentrated somewhat), a small amount of the feces, a little of the finely hashed tissue, or other material (adding a measured amount of water to the solid specimens) and add one-sixth volume of chemically pure hydrochloric acid. Place in this mixture one or two small strips of pure bright copper foil and boil the mixture for a few minutes. If mercury be present in the material examined, the copper foil will receive a gray or silvery deposit, the extent of the coating indicating something as to the relative amount of mercury present. Remove the copper foil, wash it with water followed by alcohol and ether and dry between filter paper. The mere coating of the copper is not absolute proof of the presence of mercury, as deposits will occur from arsenic, antimony, bismuth, silver, and some rare metals as well as from some organic sulphur compounds, although a bright silvery deposit is very suggestive of mercury. To prove that this deposit is mercury, cut the copper foil into small bits, place in a small dry reduction tube about 10 cm. long and 5 mm. wide and heat the lower end of the tube over a free flame in such a way that the copper glows slightly. Under these conditions the mercury will sublime and collect on the cooler portions of the tube. Microscopic examination of this sublimate will reveal the characteristic globules of mercury, which show the bright high lights under reflected light. As a further verification of mercury, shake out the bits of heated copper foil, place in the tube a crystal of iodine and stopper with a cotton plug, allowing the tube to stand for a while, when the sublimate will become red from the formation of mercuric iodide. The coatings originally present on the copper foil may sublime, if they be due to the presence of arsenic or antimony, as well as to mercury, but the appearance of the sublimate is different in each case; arsenic appearing in the form of octahedral crystals; antimony as acicular crystals; and mercury as globules. This test does not work properly if oxidizing agents, such as nitric acid, chlorate, etc. are present, so that measures should be taken to remove these if they are known to be present. This test is extremely delicate, Wormley[1] being able to obtain characteristic globules from 1/500000 grain, although usually 1/100000 grain would seem to be nearer the limit of delicacy. By a special electrolytic method of amalgamation, using microscopic examination of the deposit, Booth and Schreiber[2] were able to detect mercury in 1 drop of a solution containing 0.5 mg. per liter.

Electrolytic Test.—Various methods of depositing the mercury upon other metals by electrolysis have been advocated, some using a cathode of gilded platinum and an anode of platinum, others a cathode of copper and an anode of platinum, the current being furnished by dry cells. Such methods are extremely delicate and may be employed if such an apparatus be at hand. Probably the simplest electrolytic method is the *Galvanic Gold Test*, which is performed as follows: A band of gold foil is wrapped about a strip of thin zinc, leaving some zinc exposed, thus making a galvanic couple. Hang this gold-zinc couple in the suspected fluid, which has been acidulated with hydrochloric acid and warm. After an hour or two a silvery deposit will appear on the gold if mercury be present in the solution. This deposit may be identified as mercury by subliming as previously outlined.

Determination.—In the quantitative estimation of the mercury in the tissues, urine, feces, etc., the decomposition of the organic matter is usually carried out by the method of Fresenius and von Babo. While there is a possibility of slight loss of mercury in this process, yet this may ordinarily be disregarded provided the operations are conducted in flasks with reflux condensers and the excess chlorine is removed with a current of carbon dioxide rather than by evaporation. Palme[1] and later Lomholt and Christiansen[2] advise the oxidation with potassium permanganate in the presence of sulphuric acid, and Booth, Schreiber and Zwick[3] have introduced a method, based on this process, which is very delicate but which is too complicated for the ordinary toxicological laboratory.

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[1] *Micro-Chemistry of Poisons*, 2nd Ed., 1885, p. 351.

[2] Jour. Amer. Chem. Soc., 1925, **47**, 2625.

The usual procedure is as follows: Weigh or measure out a definite amount of the material to be examined and decompose the organic matter with hydrochloric acid and potassium chlorate in a closed flask fitted with a reflux condenser. After decomposition is complete, pass a current of carbon dioxide to remove the excess chlorine, and filter, washing the residue with hot water. Treat the filtrate with washed hydrogen sulphide for at least ½ hour, allow the precipitate to settle for a short time, wash quickly with cold water, dry at 100° C., and weigh as such.

If preferred the mercury may be determined by the method of Rose as follows: Dissolve the precipitated and washed mercuric sulphide in *aqua regia* and evaporate the solution nearly to dryness at a low temperature. Dissolve the residue in a large quantity of water and add phosphorous acid (obtained by the oxidation of phosphorus in moist air) in excess. Allow to stand over night in a cool place, collect the mercurous chloride on a weighed filter, wash with hot water, dry at 100° C., and weigh as calomel.

In the examination of urine the amalgamation tests have been employed with satisfactory results, when slightly modified, although some workers believe that the results are not exactly quantitative. Vogel and Lee[4] oxidize the organic matter by the method of Fresenius and von Babo, remove the excess chlorine with carbon dioxide and deposit the mercury upon copper wire in the usual manner. The mercury is then sublimed and collected upon weighed gold foil held in the upper portion of a narrow tube. This amalgamated gold foil may then be weighed and the amount of mercury determined from increase in weight of the gold foil; or the amalgamated gold foil may be weighed and the mercury sublimed onto the sides of a weighed dry tube and the mercury determined from the loss of weight of the gold foil after sublimation and checked by the increase of weight of the glass tube. Elliott[5] dispenses with the decomposition of the organic matter, adding fine copper powder to the acidified urine, allowing it to stand over night, filtering and washing the copper with water, alcohol and ether, and then placing this dried amalgamated copper in a special tube, in the upper portion of which is placed a weighed piece of gold foil. The mercury is then sublimed and collects on the gold foil, the increase in weight of which gives the amount of mercury in the quantity of urine examined. Schreiber, Sollmann and Booth[1] have outlined a method for the determination of mercury in urine and feces, which is extremely delicate, the details of which must be obtained from the original article.

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[1] Ztschr. f. physiol. Chem., 1914, **89**, 345.

[2] Biochem. Ztschr., 1917, **81**, 356.

[3] Jour. Amer. Chem. Soc., 1926, **48**, 1815.

[4] Jour. Amer. Med. Assoc., 1914, **62**, 752.

[5] Jour. Amer. Med. Assoc., 1917, **68**, 1693.

COPPER

Copper is found rather widely distributed in nature in the form of the metal itself, and as the ores, the oxide, carbonate, and sulphide. It is found associated with many common minerals and, thus, forms a part of many soils and is, not infrequently, a constituent of natural waters. It is present in most of our vegetables, fruits, and cereals, as, also in such sea-foods as oysters, clams, and crabs[2]. Lindow, Elvehjem, and Peterson[3] state that no food examined by them was without copper, the classes of foods in descending order of copper content being nuts, dried, legumes, cereals, dried fruits, poultry, fish, animal tissues, green legumes, roots, etc., leafy vegetables, fresh fruits, and non-leafy vegetables, oysters showing a high content and surpassing all sea foods in this element.

As it is present in so many of the foods of man and animals, it is, probably, to be regarded as a normal constituent of the animal body, although it must be remembered that some copper may find its way into the system through food artificially colored with copper salts and, also, from food contaminated with copper as a result of the solvent action of acid substances cooked or prepared in copper vessels. The presence of copper in human tissues, probably even in the new-born, is so constant, that it is the experience of practically every toxicologist to find traces of it in almost every investigation by him. Witthaus[4], for instance, remarks that "we have yet to examine a human liver which does not contain it." Palet[5], however, did not find it in 54 "normal" human livers examined by him, due, possibly, to the different diet in Argentine. Flinn and Von Glahn[6] examined 20 specimens of normal livers obtained from autopsies and found copper in amounts varying from 2.30 to 12.42 mg. per kilo. McHargue[7] has shown the presence of copper in the tissues and blood of cattle, stating that the copper content of the liver, for instance, may be very variable, depending upon the age of the animal and, possibly, upon the food source, as well as the species, while Warburg and Krebs[1] found in human serum approximately 0.0017 mg. of copper per cc., and an amount of about the same order associated with the serum proteins, these same workers reporting copper as present in the serum of such animals as the dog, cat, rat, guinea pig, frog, chicken, and goose. Hess, Supplee and Bellis[2] have shown that cow's milk and woman's milk regularly contain copper and that, in infants and adults, copper is absorbed from the alimentary tract as proved by its constant presence in the urine.

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[1] Jour. Amer. Chem. Soc., 1928, **50**, 1620.

[2] See Galippe, Ann. d' Hyg., 1883, **9**, 128; Tschirch. *Das Kupfer*, 1893; Lehmann, Arch. f. Hyg., 1897, **31**, 279; Fleurent and Levi, Bull. Soc. Chim., 1920, **27**, 440; Rose and Bodansky, Jour. Biol. Chem., 1920, **44**, 99.

[3] Jour. Biol. Chem., 1929, **82**, 465; See, also, Elvehjem and Lindow, Ibid., 1929, **81**, 435; Elvehjem and Hart, Ibid., 1929, **82**, 473; Webster and Jausma, Science, 1929, **70**, 174.

[4] *Toxicology*, 1911, p. 707. See, also, Ryan, Univ. Pa. Med. Bull., 1907, **20**, 53; Flinn, Amer. Jour. Physiol., 1928, **85**, 369; Turnwald and Haurowitz, Ztschr. f. physiol. Chem., 1929, **181**, 176.

[5] Semana medica, 1919, **26**, 151.

[6] Jour. Exp. Med., 1929, **49**, 5. See, also, Schönheimer and Oshima, Ztschr. f. Physiol Chem., 1929, **180**, 249 and 252.

[7] Amer. Jour. Physiol., 1925, **72**, 583; Jour. Ind. and Eng. Chem., 1927, **19**, 274.

Although copper, even though constantly present in the tissues, blood, and milk, has not generally been regarded as an element, which filled a physiologic requirement of the system, yet the recent work of Waddell, Elvehjem, Steenbock, and Hart[3] would seem to indicate such a possibility. It has been shown by these workers that such inorganic iron salts, as the chloride, sulphate, acetate, citrate, and phosphate, when fed at such a level that they introduce 0.5 mg. of iron daily, fail to increase materially the hemoglobin level in anemic rats, while the ashed residues from dried beef liver, dried lettuce, and yellow corn, and acid extracts of the same, when fed at the above level, are very effective in curing the anemia produced in rats by a diet of cow's milk. These facts may be explained by assuming that the ashes and ash extracts contain, in addition to iron, some other inorganic substance, or substances, vitally concerned in the building of hemoglobin. Later work by these investigators[4] has demonstrated that the ash of a preparation of beef liver as, also, the HCl extract of such ash treated with H_2S followed by ammonium sulphide, was very active, the potent factor being concentrated in the H_2S fraction. Copper, as one of the elements in this fraction, showed itself to be highly active in the curing of the anemia, or, in other words, in the building of hemoglobin. These experiments may partially explain the value of the liver diet of Minot and Murphy[5] in pernicious anemia. According to the work of Titus, Cave and Hughes[6] the combination of manganese with copper appears to produce a quicker response from the standpoint of hemoglobin building than does either copper or manganese alone.

Acute poisoning by the salts of copper is not of very frequent occurrence, although over 100 reports of alleged copper poisoning were collected by Witthaus[7] in 1911, only 42 of which were considered truly authentic.

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[1] Biochem. Ztschr., 1927, **190**, 143. See, also, Krebs, Klin. Wchnschr., 1928, **7**, 584.

[2] Jour. Biol. Chem., 1923, **57**, 725. See, also, Quam and Hellwig, Ibid., 1928, **78**, 681; Elvehjem, Steenbock and Hart, Ibid., 1929, **83**, 27.

[3] Ibid., 1928, **77**, 777; 1929, **83**, 251. See, also, McHargue, Healy and Hill, Ibid., 1928, **78**, 637; Elvehjem, Steenbock, and Hart, Ibid., 1929, **83**, 21; Waddell, Steenbock and Hart, Ibid., 1929, 84, 115.

[4] Hart, Steenbock, Waddell, and Elvehjem, Ibid., 1928, **77**, 797. See, also, Robscheit-Robbins, Elden, Sperry and Whipple, Ibid., 1928, **79**, 563 and 577; Flinn and Inouye, Ibid., 1929, **84**, 101.

[5] Jour. Amer. Med. Assoc., 1926, **87**, 470.

[6] Jour. Biol. Chem., 1928, **80**, 565. See, also, Titus and Hughes, Ibid., 1929, **83**, 463.

[7] *Toxicology*, 1911, p. 710.

Of these cases few were fatal. Although all of the salts of copper must be regarded as poisonous if taken in sufficient quantity, the usual ones employed have been the official copper sulphate (*blue vitriol, blue stone*) and the subacetate (*verdigris*). The usual method of administration of the copper salts is by mouth, yet fatal results have followed the application of copper sulphate in milk to the unbroken scalp[1] and serious poisoning has arisen from absorption through wounds or ulcerated surfaces.

There has been much discussion as to the possibility of chronic poisoning from ingestion of small amounts of copper. In times past copper salts have been widely used to color pickles, peas, beans, and certain drinks. While the French Council of Hygiene, composed of Pasteur, Poggiale, and Brouardel, reported[2] that "copper in the amounts found in canned goods is not capable of injury to health", the International Congress of Food Analysts[3] declared that "the use of copper in canned goods should be forbidden." The use of copper for coloring vegetables has been forbidden in Germany and Austria and, also, in the United States, the action in our country being based upon the investigations of the United States Department of Agriculture and the report of the Referee Board of Consulting Scientific Experts.[4] They concluded that, taking 10 to 12 mg. of copper as the upper limit of the small quantity which would ordinarily be in the greened vegetables daily consumed, even such small quantities of copper continuously taken may have an effect prejudicial to health and digestion. Drummond[5], however, in his investigations of the effects of vegetables artificially colored with copper upon rats, obtained only negative results.

Concerning the possibility of chronic copper poisoning in workers in its compounds, it is to be said that such workers are liable to a disease known as "copper colic", which differs from lead colic in that diarrhea is present instead of constipation; there is greater prostration; its duration is shorter; and the prognosis is good. After long exposure there may be functional disturbances of the muscular and nervous systems, associated with anemia and cachexia, but, as soon as the exposure ceases, the functions are usually restored and the cachexia disappears. Indeed, Milton[6] states that no symptom-complex of poisoning is found in certain copper workers, who show copper as a purplish or bluish line on the gums, whose hair turns green, and whose urine stains the ground green.

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[1] Petheö, Med. Klinik, 1924, **20,** 901.

[2] Ann. d'Hyg., 1880, 3S., **3,** 193.

[3] Ztschr. f. Nahrungsmittelchem., 1891, p. 557.

[4] See Food Inspection Decision 149, December 26, 1912; Report No. 97, U. S. Dep't of Agriculture, 1913.

[5] Analyst, 1925, **50,** 481.

[6] Buck's Hygiene, New York, 1879, **2,** 50 (cited by Holland, "Inorganic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2,** 202. See, also, Mazzi, Rass. clin. terap. sci. affini, 1928, **27,** 192 (Abs. in Chem. Abs., 1928, **22,** 4646).

Mallory, Parker and Nye[1] believe that chronic poisoning with salts of copper produces in the livers of rabbits in 6 months to 1 year a series of changes comparable to those found in the liver in hemochromatosis. Studies of clinical cases show that ordinarily it takes 15 to 25 years to produce the symptom-complex of hemochromatosis (bronzed diabetes or pigment cirrhosis), so that the cases are unrecognized by the clinician, and are, oftentimes, overlooked by the pathologist. According to Mallory, the cause of the disease seems to be connected chiefly with two different subjects, with alcohol and with an occupation involving copper. The experimental work with animals seems to demonstrate that copper inhaled or ingested is dangerous to life, although its action as a chronic poison is exceedingly slow. Hall and Butt[2] confirm the findings of Mallory and his co-workers, reporting that "chronic poisoning with copper salts over long periods produces in rabbits a pigment cirrhosis resembling closely the early manifestations of hemochromatosis in man." These workers, however, find that alcohol, administered in conjunction with copper acetate, not only fails to hasten or augment the production of pigment cirrhosis, but, also, reduces materially the storage of copper in the liver in both rabbits and white rats. Flinn and VonGlahn[3] conclude from their experiments that copper is not the cause of the pigment deposits in the liver of the rabbit, since the same change is produced when sodium acetate is given with the standard diet, and an exclusive diet of carrots causes a more rapid deposition of pigment than does copper with the standard diet. These workers were unable to find in any of their rabbits a definite cirrhosis. A spontaneous deposition of pigment occurs frequently in the livers of normal rabbits on the usual laboratory diet, according to these workers. Wood and Fitz-Hugh[4] assert that the etiologic relation of copper poisoning to hemochromatosis has not been proven; while Funk and St. Clair[5] do not believe that copper has much to do with hemochromatosis.

Symptoms.—The early symptoms of acute poisoning with copper salts are those of a marked gastro-intestinal irritation. There is an astringent taste and a feeling of tightness and constriction in the throat almost immediately on swallowing the poison. In a short time, usually within 5 or 10 minutes, but in some cases, where the stomach is full of food, not for ½ hour or even longer, there is pain in the stomach, nausea, and vomiting of greenish material, which is turned blue on the addition of ammonia. Soon the patient complains of a marked thirst, pain in the abdomen, which may be of a colicky type, associated with violent purging, the stools being liquid and brownish in color at first, but later becoming greenish.

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[1] Jour. Med. Research, 1921, **42,** 461. See, also, Mallory, Amer. Jour. Path., 1925, **1,** 117; Arch. Int. Med., 1926, **37,** 336.

[2] Arch. Path., 1928, **6,** 1.

[3] Jour. Exp. Med., 1929, **49,** 5.

[4] Arch. Int. Med., 1929, **44,** 882.

[5] Ibid., 1930, **45,** 37.

The urine is scanty, may contain albumin and blood, and later is often loaded with casts. The pulse may be full and strong early in the attack, but soon becomes weak and rapid. The respiration is accelerated and dyspneic. Later appear headache, a feeling of anxiety, vertigo, convulsions, which may be tetanic in character, paralysis of the extremities, delirium, and collapse. If death does not occur too quickly, jaundice appears, associated with pain in the hepatic region. In some cases a purplish or bluish line may be shown on the gums.

Fatal Dose.—Just how much copper sulphate or subacetate would be required to prove fatal is difficult to state, as much of that taken into the stomach is lost by the energetic vomiting which ensues. The fatal dose of copper sulphate has been given widely varying figures by different authors. Von Hasselt[1] places it at 0.4 to 0.5 gram (6 to 8 grains), while Böcker[2] gives it as 30 to 60 grams. Kobert[3] inclines to the fatal dose of 30 grams, but believes that 10 grams might kill. One fatal case from intake of 30 grams has been reported by Starr[4], while Kétli[5] records a case of recovery following a dose of 120 grams (about 4 ounces) of the sulphate. The fatal dose of the subacetate seems to be somewhat lower than that of the sulphate, as death of an adult has occurred from a dose of ½ ounce of the former,[6] while 1.25 grams (19 grains) has proven fatal to a child.[7]

Fatal Period.—Death does not, as a rule, occur for several days, Starr's case[8] dying in 4 days and 5 hours and Maschka's case[9] in 7 days, while in the case of Meerowitsch and Moissejewa[10] death was delayed till the 15th day. On the other hand, Wachholz[11] reports a case of death from spasm of the glottis "soon after having swallowed a strong solution of the sulphate" and Taylor[12] cites the death of a child in four hours from taking an unknown quantity of blue vitriol. Death from verdigris has occurred in 60 hours and, also, in 3 days.[13]

Treatment.—The stomach should be evacuated as quickly as possible, stimulating the natural effort at vomiting unless the patient is very weak. The stomach should be washed out with water containing potassium ferrocyanide in order to form the insoluble cupric ferrocyanide. This may be followed by administration of eggs beaten up in water or milk and then by removal of this from the stomach by lavage. The bowels may be cleared by high colonic flushing. If necessary to combat the collapse, stimulants may be given.

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[1] Cited by Kobert, *Lehrbuch der Intoxikationen*, 2te. Aufl., 1906, **2**, 402; and Witthaus, *Toxicology*, 1911, p. 711.

[2] *Lehrbuch der gerichtlichen Medizin*, 1857, p. 243.

[3] *Loc. cit.*

[4] Medical Record, 1882, **21**, 564.

[5] Pest. med.-chir., Presse, 1883, **19**, 310.

[6] Cited by Taylor, *On Poisons*, 3rd Amer. Ed., 1875, p. 427.

[7] Kobert, *Loc. cit.*, p. 402.

[8] *Loc. cit.*

[9] Wien. med. Wchnschr., 1871, **21**, 628.

[10] Deutsch. Ztsch. f. d. g. ger. Med., 1928, **11**, 189.

[11] Ztschr. f. Med. Beamte, 1893, **6**, 397.

[12] *Loc. cit.*, p. 433.

[13] Taylor, *Loc. cit.*, p. 427.

Postmortem Appearances.—The tongue and throat may be colored a bluish-green. The entire alimentary tract from the esophagus to the anus may be congested, swollen, ecchymotic, or even ulcerated. Occasionally, these ulcers may perforate and permit the passage of the intestinal contents into the abdominal cavity. The mucous membrane of the digestive tract may be bluish in color, although this may not be shown. Jaundice may be present and the liver, if death has not been too rapid, will show fatty degeneration and the kidneys give evidence of a parenchymatous nephritis. Occasionally the blood may appear brownish, due to formation of hematin, as in the case reported by Starr[1].

Detection.—Copper is excreted through the bile, the kidneys, the gastric and intestinal glands, and to some extent through the skin. It may be detected in these excretions and in almost all the tissues, being especially prevalent in the liver, pancreas, kidneys, brain and muscles. On account of the presence of copper in the tissues as previously mentioned, the finding of small amounts of copper in the toxicological examinations must be interpreted rather cautiously, amounts of 3 to 15 mg. per kilo of liver probably being regarded as within "normal" limits.

In the systematic method of analysis, copper is found in the precipitate produced by H_2S in the filtrate from the decomposition of the organic matter by hydrochloric acid and potassium chlorate. On extraction of this precipitate with ammonium sulphide to separate the metals of the arsenic group, a portion of the copper will probably pass into this solution, while some will remain in the insoluble residue. The presence of copper in these portions may be shown by the usual methods of qualitative analysis, the blue color given by copper solutions in the presence of ammonia and the reddish-brown coloration or precipitation of copper ferrocyanide being especially valuable qualitative tests.

Determination.—A weighed portion of the finely hashed tissue, or a measured amount of the gastric contents, is treated with hydrochloric acid and potassium chlorate or by the method of Gautier to decompose the organic matter and the solution treated as discussed on page 342. Heat the filtrate to incipient boiling and saturate the solution with hydrogen sulphide, allowing the flask to stand on a steam bath for a few minutes until the copper sulphide flocculates. Filter and wash the precipitate at once with hydrogen sulphide water. Place the filter containing the copper sulphide precipitate in a small flask, add 4 to 5 cc. of concentrated sulphuric acid and the same quantity of strong nitric acid, and heat until white fumes appear. Continue the oxidation, adding a little strong nitric acid from time to time, until the liquid remains colorless upon heating to the appearance of white fumes. Cool, dilute with about 30 cc. of water, add an excess of bromine water, and boil until all bromine is expelled. Remove from the heat and add a slight excess of strong ammonium hydroxide and boil until the excess of ammonia is expelled. Now add a slight excess of strong acetic acid (3 or 4 cc. of 80 per cent. acid) and boil for a minute. Cool to room temperature and add 10 cc. of 30 per cent. potassium iodide solution and titrate at once with N/10 sodium thiosulphate solution until the brown tinge has become weak and then add sufficient starch indicator to produce a marked blue coloration. Continue the titration cautiously until the color due to free iodine has entirely vanished. One cc. of the thiosulphate solution represents 0.0063 gram of copper or 0.01596 gram of anhydrous copper sulphate or 0.02497 gram of crystallized copper sulphate.[1]

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[1] Medical Record, 1882, **21**, 564.

BISMUTH

Poisoning with the compounds of bismuth is relatively infrequent, owing to the fact that, when given by mouth, these compounds are very slightly absorbed. When such compounds are applied to abraded surfaces, such as burns or suppurative sinuses, the absorption is more rapid and complete, so that the signs of poisoning in such cases may appear in a short time.

The salts of bismuth are widely used in medicine, being given as local sedatives for gastric and intestinal irritation, while formerly very large doses were employed as contrast meals in X-ray work. In later years bismuth has found somewhat extensive use in the treatment of chronic suppurative sinuses and empyema by the local injection of bismuth-vaseline paste and several organic compounds of bismuth are now employed in the treatment of syphilis. The official salts of bismuth are the subcarbonate, subgallate, subnitrate and subsalicylate, while we find in New and Nonofficial Remedies such organic preparations as bismosol (a sterilized solution of potassium sodium bismuthotartrate 10 grams, piperazine 0.3 gram in sufficient aqueous solution of glucose to make 100 cc.), potassium bismuth tartrate, bismuth sodium tartrate, mesurol (basic bismuth-methoxy-hydroxy-benzoate), and oleo-bi-roche (a suspension of finely divided bismuth oleate in olive oil), all of these being given by intramuscular injection.

In the earlier cases of reported poisoning with bismuth salts, especially the subnitrate, it is probable that most of the fatal results were due to the presence of arsenic as an impurity, while some cases may have been due to contamination with antimony as well. Occasionally, tellurium has been found as an impurity[2], the so-called "bismuth breath," a peculiar garlic-like odor, probably being attributable to this source. According to Higgins[3], the records of all methods of internal administration of bismuth compounds show 21 toxic cases with 14 fatalities. In cases in which bismuth has been used for the treatment of burns and as surgical antiseptics quite a few non-fatal poisonings have been reported, while several deaths[1] have occurred. Since the introduction of the so-called "Beck paste"[2] (bismuth vaseline paste) in the treatment of suppurative sinuses, at least 70 toxic cases with 26 deaths have been reported[3], although Beck[4] draws attention to the fact that he has treated a series of 1800 cases with this paste without a single fatality, maintaining that the mishaps reported are due to the surgeon's carelessness and faulty technic or to the patient's idiosyncrasy. In such cases, when a blue gingival line and stomatitis appear, which is certain evidence of absorption of the bismuth, prompt and thorough removal of the paste from the sinus is indicated. In this connection it should be mentioned that, during the World War, a somewhat similar bismuth paste, called "bipp" consisting of 1 part of bismuth subnitrate, 2 parts of iodoform, and 1 part of liquid paraffin, was applied in the British service to infected wounds, Morison[5] reporting that out of hundreds so treated only 3 had "blue gum" with stomatitis attributable to absorbed bismuth, and of these there were no fatalities.

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[1] See Rose and Bodansky, Jour. Biol. Chem., 1920, **44**, 99; and Currie, Biochem. Jour. 1924, **18**, 1224 for delicate quantitative tests for small amounts of copper.

[2] See Reisert, Amer. Jour. Pharm., 1884, **56**, 177; and Braithwaite, Amer. Druggist, 1884, **13**, 88.

[3] Jour. Amer. Med. Assoc., 1916, **66**, 648.

In some cases, especially in infants, poisoning has occurred from the reduction of the bismuth subnitrate to the nitrite under the influence of the bacteria of the intestinal tract. Such cases do not show the symptoms of bismuth poisoning, but, rather, those of nitrite intoxication characterized by cyanosis, diarrhea, dyspnea, collapse, and death from paralysis of respiration, such a chain of symptoms, probably, being attributable to methemoglobinemia.[6] Quite a number of poisonings of this type have occurred with at least 6 deaths, although Lewin[7] denies that there is nitrite action in such cases.

In the use of the intramuscular injection of the organic bismuth compounds in syphilis, toxic effects are not uncommon and death has resulted[8], although prompt suspension of the treatment is, usually, followed by recovery, if close attention is paid to the appearance of such signs of absorption as salivation, blue-black line at the gingival margins, stomatitis with black spots in the mouth, etc. Owing to the fact that the injection of some of these bismuth compounds is associated with more or less induration, which remains for sometime as evidence of slow, uncertain, or irregular absorption of the bismuth[1], cumulative effects may appear following a series of subtoxic doses, such being indicated by headache, malaise, weakness, albuminuria, and jaundice. The intramuscular injection of bismuth sodium tartrate (water-soluble) brings about a prompt and sustained diuresis in subjects with and without edema, without demonstrable local or systemic reactions and, apparently, without injury to renal function.[2]

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[1] See Gaucher and Balli, Bull. et mém. Soc. méd. des hôp. de Paris, 1895, 3s., **12**, 781; Mahne, Münch. med. Wchnschr., 1905, **52**, 193; Eggenberger, Centralbl. f. Chir., 1908, **35**, 1309 and 1537.

[2] Beck, Ill. Med. Jour., 1908, **13**, 402; Jour. Amer. Med. Assoc., 1909, **52**, 14; Ann. Surg., 1914, **59**, 145.

[3] See Mayer and Baehr, Surg., Gyn., and Obst., 1912, **15**, 309; Holland, "Inorganic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 205; Torrione, Schweiz. med. Wchnschr., 1928, **58**, 895.

[4] Jour. Amer. Med. Assoc., 1916, **67**, 21.

[5] Brit. Jour. Surg., 1917, **4**, 659.

[6] See Bennecke and Hoffman, Münch. med. Wchnschr., 1906, **53**, 945; Böhme, Arch. f. exp. Path. u. Pharm., 1907, **57**, 441; Meyer, Therap. Monatsh., 1908, **22**, 388; Nowak and Gütig, Berl, klin. Wchnschr., 1908, **45**, 1764; Barabaschi, Gazz. d. osp., 1908, **29**, 1169; Zollinger, Jour. Amer. Med. Assoc., 1912, **58**, 901.

[7] Münch. med. Wchnschr., 1909, **56**, 643.

[8] See Villanova, Ann. des Mal vénér., 1925, **20**, 25; Munck, Dermat. Wchnschr., 1927, **84**, 367.

Symptoms.—While the administration of bismuth salts by mouth is not ordinarily associated with any uncomfortable signs, yet, when toxic doses have been taken the patient may complain of a peculiar, metallic taste, which is soon accompanied by salivation, foul breath, stomatitis with black spots in the mouth and throat and a blue line along the gingival margin. There may be vomiting with rather marked abdominal pain, diarrhea with stools of dark color from formation of bismuth sulphide. Later a nephritis develops, the urine being dark in color aind showing albumin and casts in large numbers. The irritation in the intestinal tract may be so marked that the ulcers perforate, peritonitis following as a result. As previously stated, the absorption of bismuth is more rapid and complete from abraded surfaces than from the intact gastro-intestinal mucosa, the above symptoms may be more marked following other methods of administration than the oral route. Bismuth is eliminated by the urine, saliva and hair.[3]

Fatal Dose and Period.—The minimum fatal dose of bismuth subnitrate or of the other official salts is difficult to determine, as most of that taken into the stomach is not absorbed, but is eliminated by the gastro-intestinal tract. After absorption, elimination occurs through the saliva and urine. As the absortion of bismuth given by parenteral routes is greater, the medicinal dose, as well as the toxic dose, is much smaller under these conditions. On account of the frequent occurrence of arsenic as an impurity in bismuth salts, the earlier reports as to the fatal dose must be taken with some allowance. A much quoted case is the one cited by Taylor[4] of death in 9 days from a dose of 2 drams (7.7 grams) of the subnitrate, while he mentions, also, recovery from a dose of 6 drams (23 grams). In the case reported by Munck[5] a man received within 11 months the equivalent of 5.13 grams of metallic bismuth in the course of treatment for syphilis. Death occurred 12 days after the onset of toxic symptoms of jaundice and stomatitis.

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[1] See Erdman, Jour. Amer. Med. Assoc., 1929, **92**, 1252; and Boyd, Ibid., 1929, **93**, 269.

[2] See Hanzlik, Bloomfield, Stockton, and Wood, Jour. Amer. Med. Assoc., 1929, **92**, 1413.

[3] See Fabre and Picon, Jour. pharm. chim., 1928, **8**, 249 & 297; Ibid., 1929, **9**, 97.

[4] *On Poisons*, 3rd. Amer. Ed., 1875, p. 469.

[5] Dermat. Wchnschr., 1927, **84**, 367.

Treatment.—In the acute cases the bismuth should be removed from the stomach by repeated lavage, while that in the intestinal canal should be washed out by high colonic flushings and the administration of castor oil. Further treatment should be purely symptomatic. In the cases following the use of the organic preparations of bismuth, prompt suppression of further treatment on the first appearance of buccal irritation will usually result in recovery.

Postmortem Appearances.—The most striking lesions seem to be the brownish-purple spots on the tongue, the mucosa of the mouth and throat, and the blue line along the gums. The teeth may be loose and the gums spongy from the intense salivation and stomatitis. The appearances in the stomach and intestines closely resemble those noted in mercury poisoning, the ulcers occasionally being extensive and occasionally perforating. The liver may show hyperemia and parenchymatous hepatitis, while signs of parenchymatous nephritis are almost constantly present in fatal cases. Owing to the destruction of red blood cells, hemosiderin deposits may be noted in the spleen, liver, kidneys, and mucosa of the large intestines.

Detection.—In the systematic process of examination of tissues for inorganic poisons, bismuth is found in the precipitate formed by treatment of the filtrate, from the decomposition of organic matter by the method of Fresenius and von Babo or the Gautier method, with H_2S. On treatment of this precipitate with ammonium sulphide to remove the sulphides of the arsenic group, bismuth along with other sulphides will be left in the insoluble residue. On now treating this insoluble residue of sulphides with dilute nitric acid, all of these will dissolve with the exception of the mercuric sulphide. Filter this nitric acid solution of the sulphides to remove the mercury and any sulphur formed and apply the usual qualitative tests for bismuth, the precipitation of the hydroxide with excess of ammonium hydroxide being of great value. If this bismuth hydroxide be dissolved in a few drops of hydrochloric acid and a large amount of water added, an immediate precipitation of the oxychloride of bismuth forms, which is very characteristic.

Determination.—In the quantitative determination of bismuth, a weighed portion of the finely hashed tissue is treated with water and decomposed by the method of Fresenius and von Babo, or, as some prefer, the Gautier method, owing to the possibility that some of the bismuth chloride formed in the former process may be volatilized. The filtrate from either process is treated with H_2S and the sulphide allowed to settle out. After a short time filter off the precipitate and wash it with water containing hydrogen sulphide. The washed precipitate of bismuth sulphide may be weighed as such, or the determination may be made either as metallic bismuth or as the trioxide, the writer preferring the latter method. Dissolve the bismuth sulphide in nitric acid and add ammonium carbonate solution in very slight excess. Now heat for some time nearly to boiling, filter off the precipitate of bismuth carbonate, dry in the oven and ignite carefully in a weighed porcelain crucible until the weight remains constant, in order to convert the carbonate into the trioxide. If the weight of the trioxide be multiplied by 0.8966 the result will be the amount of metallic bismuth in the weighed portion of tissue taken for examination.

It is often of importance to examine urine for the presence of bismuth, especially in cases of administration of organic preparations in syphilis. For qualitative purposes the method of Aubry[1] may be employed. Add some ammonium nitrate to the urine and evaporate to dryness, ash carefully and dissolve the residue in dilute nitric acid. To this solution add about twice the amount of the following reagent (1 gram quinine sulphate, 3 or 4 drops of concentrated sulphuric acid, 2 grams of pure potassium iodide, water to make 100 cc.), when an orange-red precipitate will form in the presence of bismuth, a coloration being visible in a dilution of 1 part of bismuth trioxide in 600,000. For quantitative determination of the bismuth in the urine the method of Hill[2] gives excellent results. Destroy the organic matter by heating with nitric acid, repeating the evaporation with nitric acid until oxidation is complete. Evaporate to a small volume, add 0.3 gram of urea and 0.5 gram of phenazone and, while shaking, add about 0.005 gram of potassium iodide crystals one at a time until the maximum color develops. Make up the volume to 50 cc. in a volumetric flask. Compare the color in a colorimeter with a standard solution of bismuth prepared as follows: Weigh out 0.62 gram of bismuth carbonate, add a little water and 10 cc. of strong nitric acid and make up to 1 liter. Dilute 10 cc. of this solution to 1 liter and take 10 cc. of this diluted standard, which amount represents 0.05 mg. bismuth, add 1 drop of nitric acid and the urea, phenazone and potassium iodide as specified for the unknown solution and make up the volume to 50 cc. Make the color comparisons in a colorimeter.

ARSENIC

Occurrence.—Arsenic occurs in nature in the free state, usually in the form of mamillated masses, although, occasionally, it is met with in distinctly crystalline form. It is, however, much more commonly found in the state of combination in ores and minerals, as, for instance, arsenical iron (FeAs), arsenical nickel (NiAs), sulpho-arseniuret of nickel (NiSAs), sulpho-arseniuret of cobalt (CoSAs), arsenical pyrites (FeSAs, mispickel), realgar (arsenous sulphide, As_2S_2), and orpiment (arsenic sulphide, As_2S_3). Besides these truly arsenical minerals, arsenic is found as an impurity in many other minerals, especially worthy of mention being iron pyrites, which may be a source of arsenic in sulphuric acid and ferrous sulphide, which may lead to the introduction of arsenic into analytical determinations, if care is not taken to exclude it. Small amounts are found in many specimens of lignite, coal and shale, while native sulphur not infrequently is contaminated with it. Taking this rather wide distribution of arsenical minerals into consideration, it is not suprising to find that some virgin soils and some natural mineral waters contain traces of arsenic, while sea water, marine algae and higher plants often show quite appreciable amounts.

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[1] Jour. pharm. chim., 1922, **25**, 15. See, also, Labat et Pery, Bull. soc. pharm. de Bordeaux, 1923, **61**, 231; and Fabregue et Bressier, Jour. pharm. chim., 1924, **30**, 11.

[2] Lancet, 1925, **2**, 1281. For another method see Baggesgaard-Rasmussen, Jackerott and Schou, Biochem. Ztschr., 1928, **193**, 53.

Metallic arsenic is not infrequently found as an impurity in commercial zinc and iron, while its presence in lead and antimony may lead to its appearance in shot and bullets and, also, in such alloys as Babbitt and Brittania metals. Its presence in tin and solder may lead to arsenic being taken up by food products from cans made of impure tin, Jenkins[1] reporting a case of arsenic poisoning from sardines contaminated by arsenic from such a source. It is to be remembered that arsenic is found in both sulphuric and hydrochloric acids, so that great care must be taken in toxicological work to insure the freedom of these acids from arsenic before making any tests for this element.

Experiments by Paschkis and Obermayer[2] have shown that elementary arsenic, free from oxidation products, may be absorbed by the skin and undergo oxidation in the body with the production of symptoms typical of arsenic poisoning. Kobert[3] has noted the same thing with reference to the allotropic form (yellow arsenic, As_4) dissolved in oil. Arsenic, when exposed to moist air, is partly oxidized to a brownish-black powder, which is known as "cobalt" and is used as a constituent of fly poisons or fly paper, Witthaus[4] stating that 24 cases of poisoning have occurred from this source, of which 7 were homicidal, 2 suicidal, 8 accidental, and 7 uncertain. Twenty-two other cases of accidental poisoning of children from this source were reported, 8 of which were fatal[5]. When arsenic is volatilized by heat, vapors of arsenous oxide form, so that grave danger arises in the smelting and purification of arsenical ores.[6]

In Coal Products.—The presence of arsenic in coal, coke, lignite, etc. may lead to a type of chronic arsenical poisoning, known as "Pitch disease" of the pitch and briquet industry as shown by Bayet and Slosse[7], a condition which may occasionally be observed in chimney sweeps, boiler cleaners, soot packers, gas, coke and tar workers. Taylor and Trubshaw[8] cite 6 cases of arsenical poisoning caused by fumes from a coke stove.

In the Air.—Whenever nascent hydrogen acts on reducible arsenical compounds arsine (arseniuretted hydrogen) is formed, which is the most deadly of the inorganic compounds of arsenic. Many fatal cases of poisoning have arisen from this source, but the discussion will be taken up in the chapter devoted to Gaseous Poisons. In addition to this source of contamination of the air, we find that combustion of certain coal products often leads to the throwing off of arsenical vapors, which may prove toxic, cases of both acute and chronic types being noted.

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[1] Med. Herald, 1882–83, **4**, 17.

[2] Med. Jahrb. 1888, **3**, 117.

[3] *Lehrbuch der Intoxikationen*, 2te. Aufl., 1906, **2**, 244.

[4] *Toxicology*, 1911, p. 383.

[5] Editorial, Jour. Mich. State Med. Soc., 1915, **14**, 580.

[6] See Salmon, Am. Vet. Rev., 1911, **39**, 14.

[7] Bull. acad. roy. med. Belge, 1919, **29**, 607; C. R. Acad. des Sci., 1919, **168**, 704.

[8] Brit. Med. Jour., 1911, **2**, 1591.

In Preservatives, Insecticides and Vermin-killers.—Very frequent employment is made by taxidermists of arsenical soaps and of arsenical powders to preserve the skins of animals, so that such workers have suffered from poisoning arising from this source, while it is not impossible for toxic effects to occur from the arsenic volatilized from stuffed animals. In some sections of the country it is quite common practice to spray orchards and food plants with lead arsenate, calcium arsenite, or Paris green to overcome such pests as the gypsy moth, twig borer, potato bug, etc. A possibility certainly arises of a combination of chronic lead and arsenic poisoning or of pure arsenic poisoning from the eating of the fruit or vegetables, which have not been properly washed. Of course when such preparations are used on the tops of plants, the edible portions under the ground may not be greatly affected, but where the tops are eaten the danger is one to be considered. Arsenical preparations are sometimes used in the form of a "sheep dip" to destroy parasites in wool, so that toxic effects may be experienced by those working with such processes. Probably the most extensively used vermin-killer is "Rough on Rats" and similar preparations, which consist of a mixture of a little lampblack with arsenous oxide (50 to 70 per cent.) and barium carbonate (30 to 50 per cent.), the composition of the powder varying from time to time depending on the market price of the constituents. This poisonous material may be easily obtained from any drug store without any questions being asked, so that it has found a wide vogue both for suicidal and homicidal administration.

In Common Pigments.—The most common arsenical pigments are Scheele's green (copper arsenite, $CuHAsO_3$)[1] and Paris green[2] (Schweinfurth green, emerald green, copper aceto-arsenite $(C_2H_3O_2)_2$ Cu. 3Cu $(AsO_2)_2$). The former is a pale green powder containing 52.8 per cent. of white arsenic, while the latter is a bright green crystalline powder, containing 58.55 per cent. of arsenic trioxide.

These arsenical pigments, especially the Paris green, have been used for both homicidal and suicidal purposes, Witthaus[3] stating that he has knowledge of some 26 cases of homicidal poisoning, or attempts at such, during the years 1879–93, while such cases are a matter of record in both France and Germany. In New York City in the years 1867–1880, of 604 suicides by poison, 230 were by Paris green. The accidental poisonings by these arsenical greens have been of both the acute and chronic types. It is impossible to give any reliable figures as to the extent of such cases, as only a small percentage of them find their way into the literature. Poisonings have occurred among workers in plants producing Paris green, the New York Industrial Commission[1] finding that the dust inhaled and that lodged on the skin was gradually absorbed and produced toxic effects. Accidental poisoning has occured from the use of the pigment as an insecticide, from its use as a color for candy, from children sucking articles colored therewith, from wearing articles of dress colored with arsenical greens, from drinking wine contaminated with arsenic from the green sealing-wax with which the bottles were sealed, and as a consequence of inhabiting rooms, the walls of which have been papered or painted with materials containing arsenic. There have been many authentic cases arising from all of these sources, as well as from others, although the possibility of poisoning from wall-paper or paints in living rooms has been questioned by some. However the number of cases of peripheral neuritis, skin manifestations, and even death, that have been reported in persons living in such rooms, leaves little doubt as to the source of the intoxication. The quantity of arsenic trioxide, which may be extracted from these arsenical wall-papers, may vary from a mere trace to as much as forty grains to the square foot according to Witthaus. It must be remembered, in this connection, that the color of the paper is no indication of its arsenical content, as the red, pink, blue and brown pigments, as well as the greens, may contain arsenic, the poison finding its way from the wall to the system of the inhabitant either by mechanical detachment of minute particles, which float in the dust of the room, or by the generation of a volatile or gaseous compound of arsenic. This gaseous compound was, for a time, thought to be arsine, but it has been shown by Biginelli[2], and confirmed by Maasen[3], to be diethylarsine, which is produced by the action of common molds growing in the presence of arsenical compounds. While *Penicillium brevicaule* is more active than the other molds in producing this effect, as shown by Gosio,[4] yet Schmidt[5] found 13 species of mold acting similarly, among these being *Mucor mucedo, Aspergillus vivens, and Penicillium glaucum.*

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[1] See Bornemann, Ztschr. f. allg. Chem., 1922, **124**, 36.

[2] The name "Paris Green" is probably a local one in the United States as the so-called *vert de Paris* or *Pariser grün* is, in reality, an aniline color.

[3] Toxicology, 1911, p. 578. Witthaus gives an extensive bibliography of the cases of poisoning by these pigments.

These arsenical pigments have been used in such industries as the paint and wall-paper trades, in coloring various articles, such as toys, book-covers, artificial flowers, and such dress goods as calicoes, cretonnes, chintzes, and tarlatans. Arsenic has been found in silk, in the leather bands in hats, in brown papers, glazed paper and card board used for boxes, playing cards, and note paper. In certain of the red aniline dyes, arsenic pentoxide has been used as an oxidizer, so that some of these may find their way into the market without sufficient purification and such articles of clothing as stockings and gloves may be colored by them and lead to mild symptoms of arsenic intoxication. The actual amount present in most of the above articles is now regulated by law, so that toxic effects will be less frequent.

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[1] Special Bull. 83, New York State Dep't. of Labor, 1917.

[2] Atti R. Acad. dei Lincei, 1900, (5), **9**, Pt. 2, 210 and 242.

[3] Arb. d. Kais. Gesundheitsamte, 1902, **18**, 475.

[4] Arch. ital. de Biol., 1892, **18**, 253; Ber. d. d. chem. Ges., 1896, **29**, 2728; 1897, **30**, 1024.

[5] Dissertation, Erlangen, 1900.

In Medicinal Preparations.—Arsenic in its various forms is rather widely employed in medicine and poisoning has probably occurred from all of the official compounds, as well as from many salts, which are not official. The organic compounds of arsenic are extensively used in the treatment of syphilis and other conditions and most of these have caused fatal intoxication, but their discussion will be taken up later.

Arsenic Trioxide (*Arsenous oxide, white arsenic,* As_2O_3).—This occurs as a white powder, or irregular masses of two varieties, one amorphous, transparent, and colorless, like glass; the other, crystalline, opaque and white, resembling porcelain. Contact with moist air gradually changes the vitreous into the opaque variety. It is often found as a heavy white powder, partly amorphous, partly crystalline, prepared from the vitreous variety by grinding. The crystalline "flowers of arsenic", obtained by subliming and condensation, consists of octahedral crystals. Owing to the variability in the size of the particles of white arsenic and the difference in solubility of the different forms on the market, the 10th revision of the Pharmacopoeia makes the following statements: "Powdered Arsenic Trioxide when administered in solid form, as in powders, tablets, and pills, must consist of particles not greater than 0.0125 mm. in diameter . . . The fine degree of subdivision of the powdered form of this arsenic trioxide renders it more soluble and therefore more effective than the powder previously official. This should be borne in mind in adjusting the dosage."[1] Arsenic trioxide is slowly soluble in water, the amorphous or glassy variety being somewhat more soluble than the crystalline. It is slightly soluble in alcohol and ether, and freely soluble in glycerin. It is dissolved by hydrochloric acid and by solutions of alkali hydroxides and carbonates, so that conditions are right for absorption in both the stomach and bowels. When mixed with water or such aqueous solutions as milk, coffee and tea, white arsenic floats on the surface to some extent, so that it might be detected if an attempt is made secretly to administer it in this manner. The arsenous oxide has no odor and practically no taste, so that it would hardly be noticed when mixed with food, except for its somewhat gritty property. When this oxide is administered in the solid form, it is absorbed somewhat slowly, and, in cases of rapid death from such administration, some crystals may usually be found adherent to the mucous membrane of the stomach or mixed with the food residue. The search for these crystals should always be made, as their presence throws some light on the method of administration of the poison. If solid arsenic trioxide is found, this is evidence that it was taken in that form, as it could not be thrown out of actual solution in the acid contents of the stomach. While this point may seem trivial, yet it has been raised in at least one legal investigation[1].

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[1] In this connection see Schwartze, Jour. Pharm. and Exp. Therap., 1922, **19**, 258; Ibid., **20**, 181. Also, Anderson and Story, Jour. Am. Chem. Soc., 1923, **45**, 1102.

Arsenic trioxide is present to the extent of 1 per cent in the official *Liquor acidi arsenosi* (hydrochloric solution of arsenic, solution of arsenic chloride) and *Liquor potassii arsenitis* (Fowler's solution). *Sodii arsenas* and *Liquor sodii arsenatis* (Pearson's solution) are no longer official.

Arsenic Tri-iodide (*Arseni iodidum, arsenous iodide*).—This is an orange-red, inodorous, crystalline powder, stable when protected from direct sunlight and kept in a cool place. It is soluble in about 12 parts of water at 25° C. with partial decomposition to arsenous and hydriodic acids and iodine. It is soluble in alcohol, chloroform, ether, and carbon disulphide. This compound of arsenic is present to the extent of 1 per cent along with 1 per cent of mercuric iodide in the official *Liquor arseni et hydrargyri iodidi* (Donovan's solution).

Besides the above official medicinal preparations of arsenic, this poison is found in some of the common drugs and chemicals to which the public has easy access and from which at least mild, if not fatal, poisoning may arise. Thus, arsenic has been detected in the common baking soda (sodium bicarbonate)[2], which is so widely used in the household; in bismuth subnitrate[3]; in glycerin[4]; in sodium sulphate[5]; in magnesium sulphate[6]; and in liquor ferri chloridi[7]. The arsenic in these substances is, of course, small in amount, but it may be sufficient to cause at least mild poisoning. However, when arsenic is found in appreciable amounts in the stomach and tissues, such a finding is hardly consistent with legitimate medicinal administration, as it is not ordinarily administered in amounts greater than 0.006 gram ($\frac{1}{10}$ grain) three times daily, so that one would not expect to find "more than 0.03 gram ($\frac{1}{2}$ grain) of unabsorbed arsenic in the stomach" and be justified in explaining its presence on the basis of justifiable administration.

White arsenic has, unquestionably, caused more destruction of life than any other poison, with the exception of opium and its derivatives. It has, as a rule, been administered by mouth, but quite a few cases are on record of death from external application of arsenical pastes in the treatment of cancer, and, occasionally, it has proven fatal by introduction into the vagina. It is impossible to give any exact statement of the number of deaths caused by arsenic, either homicidal, suicidal or accidental, as a very large number of such cases do not find a place in the records. Witthaus[1] states that "in 1000 cases collected at random and extending over the period from 1752 to the present time (1911), 426 were homicidal, 230 were suicidal, 200 were accidental, 33 to produce abortion, 4 through administration by quacks, and in 107 the motive is not stated." While these figures would seem to indicate that homicidal administration of arsenic is accountable for more deaths than are the suicidal and accidental methods, yet such is not in reality the case, owing to the fact that the latter type of case is not reported unless it presents some unusual feature. There have been several individuals, who have used arsenic to accomplish their purpose and who have not been suspected until suspicion was directed toward them by the number of apparent victims of similar deaths. Thus, Frau van der Linden[2] is supposed to have poisoned some 70 individuals in Leyden, among whom were her father, mother, and son; Mrs. Robinson, of Somerville, Mass., within a period of 18 months poisoned in succession 5 members of her own family without exciting any suspicion until her 6th victim died[3]; Mrs. Sherman[3], of New Haven, Conn., succeeded in escaping suspicion while she killed 3 husbands and 8 other persons of her immediate household with arsenic, the peculiar death of her 4th husband leading to her conviction. Mrs. Vermilya of Chicago poisoned 3 intended husbands with arsenic, in order to collect insurance which had been made out in her name, and was not suspected until she fatally poisoned a 4th victim. While she was under police surveillance she attempted to commit suicide by taking arsenic from her "pepper box" and was unsuccessful largely because she took too large a dose, vomiting coming on at once and much of the ingested arsenic being lost in this way. The late Prof. Haines and the writer found in the second and third vomitus (the first not having been saved) two heaping tablespoonsful of what proved to be "Rough on Rats", and yet Mrs. Vermilya suffered only the chronic effects of arsenical poisoning. Mrs. Lindloff, also of Chicago, poisoned several of her children and 1 husband with arsenic for the purpose of collecting insurance on their lives. It was not until the insurance company became suspicious of the death of the 4th child, that investigation proved that all of the children and the husband had been poisoned with arsenic.

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[1] See *Reg. v. Sturt*, Lewes Lent Assizes, 1863. Cited by Taylor, *On Poisons*, 1875, p. 319.

[2] See Mylius, Pharm. Centralh., 1886, n. F., **7**, 268.

[3] See Coad, Amer. Chem., 1875, **6**, 44, who found 0.33 per cent of elementary arsenic in a sample of bismuth subnitrate; Salisbury, Chic. Med. Jour. and Exam., 1878, **36**, 601, who found arsenic in 13 out of 18 samples of this salt.

[4] See Jaroschi, Prag. med. Wchnschr., 1889, **14**, 308; Barton, Jour. Amer. Chem. Soc., 1895, **17**, 883, and Bordas, C. R. Acad. des Sci., 1904, **139**, 234.

[5] Cameron, Analyst, 1887, **12**, 32.

[6] Rattinger, Pharm. Jahresb., 1883–84, p. 515.

[7] Buchner, Chemiker Ztg., 1887, **11**, 417.

Quite a number of so-called "mass poisonings" with arsenic have occurred, in which many individuals have been affected. Thus, in the "Bradford lozenge case" more than 200 persons were poisoned and 21 died from the mistake of the druggist in supplying white arsenic instead of ground gypsum to a manufacturer of lozenges[1]; in the Würzburg poisonings[2], 400 persons were severely poisoned by eating cakes into the dough of which arsenic was mixed; in the Manchester beer cases, it was estimated[3] that 2000 cases of poisoning had occurred from drinking beer contaminated with arsenic, which arose from the impure sulphuric acid used in the manufacture of glucose and invert sugar employed in the beer, this H_2SO_4 containing 14 grams of arsenic per liter while the beer contained from 2 to 4 mg. per liter. Taylor[4] mentions the poisoning of 340 children in an Industrial School near London, the arsenic arising from a cleaning fluid which had been introduced into a copper boiler in which the water used to dilute milk was heated. In Hyères, France, some 475 individuals were poisoned with wine contaminated with arsenic introduced accidentally, the wine containing as much as 0.16 gram per liter[5]. In Chicago a few years ago, a cook in one of the leading clubs of the city introduced arsenic into the soup, which was served at a large dinner attended by many prominent citizens, over 250 of whom were acutely poisoned, but no fatalities occurred.

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[1] *Toxicology*, 1911, p. 413.

[2] See Amer. Jour. Med. Sci., 1886, **118**, 614; Zaaijer, Vrtljschr. f. ger. Med., 1886, n. F., **44**, 249.

[3] Cited by Holland, "Inorganic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 207.

In Food.—It has been shown by Headden[6] that arsenic may be introduced into the soil by the use of "superphosphate" as manure, the arsenic arising from the impure sulphuric acid used in its manufacture; that Paris green, sprinkled on potato, cabbage, or beet plants, adds some arsenic to the soil; that the spraying of orchard trees with lead arsenate or calcium arsenite furnished a soluble fraction of arsenic to the ground and the rootlets absorb it. He found, further, that potatoes, turnips, beets, oats, alfalfa, apples, pears, and the flesh of cattle raised on a soil so treated, all gave signs of arsenic on examination. Gautier and Clausmann[7] have found that meats, milk, eggs, fish, shell-fish, vegetables and sea-water all contain arsenic and estimate that each inhabitant of Paris receives 7.66 mg. of arsenic per annum in his food. Findings of the Paris Laboratory of Toxicology are much along the same lines. While such amounts are very small and arise, undoubtedly from the wide use of arsenic in treating the soil as above mentioned, yet they may have some bearing on the subject of the so-called "normal" arsenic which will be discussed later.

In Embalming Fluids.—Another possible source of arsenic, with which the toxicologist is concerned may arise from its use in embalming fluids. In many of our states, the use of arsenical embalming fluids is prohibited by law, while in about ½ of them there is no such restriction. It may happen, therefore, that a body is embalmed with such a fluid, so that the arsenic will be found in all the tissues. There is no method by which such arsenic may be distinguished from that actually associated with homicidal or other poisoning, so that the possibility of detecting a case of arsenical poisoning by chemical means is out of the question if the body be embalmed with arsenical fluids prior to the obtaining of the organs for examination. In all suspicious cases, embalming should not be permitted until after an autopsy if possible, but in many cases, especially in those in which there may be a homicidal element, interested parties may rush the embalming in order to confuse the investigations, which will probably follow.

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[1] Pharm. Jour. and Trans., 1858–59, **18**, 340, 351 and 390.

[2] See Seisser, Aerztl. Int.-Bl., 1869, **16**, 45.

[3] See Niven, Lancet, 1900, **2**, 1752; 1901, **1**, 570; and Reynolds, Med.-Chir. Trans., 1901, **74**, 409.

[4] *On Poisons,* 3rd Amer. Ed., 1875, p. 291.

[5] See Cougit, Ann. d' Hyg., 1888, 3s., **20**, 348.

[6] "The Occurrence of Arsenic in Soils, Plants, Fruits and Animals," Proceedings of the Colorado Sc. Soc., vol. 9, p. 345.

[7] C. R. Acad. des. Sci., 1904, **139**, 101.

In most states, there is a requirement that a special record be kept of all purchases of arsenic and that the druggist insert in this record the name of the purchaser, or at least the name given to him as the purchaser. In this connection a recent ruling of the Illinois Supreme Court is of interest. This Court held[1] that a druggist's memorandum of a sale of arsenic bearing the accused's name as the purchaser was not admissable as original evidence, but it was proper for the maker as a witness to use it to refresh his memory and, after doing so, to testify to such facts as he was then able to remember. In this case, the druggist did not know the name of the purchaser, but inserted in the memorandum the name the unknown purchaser chose to give him. It was held error to admit the memorandum in evidence, and there was no evidence connecting the accused with the purchase of arsenic.

Normal Arsenic.—In 1899 Gautier[2] presented the first of a series of papers to the French Academy in which he claimed that arsenic was a normal and constant constituent of the thyroid, mammary glands, brain, thymus, hair, skin, milk and bones of man and of herbivorous and carnivorous animals, the amounts present being small and variable. Later, Gautier stated that in more than 200 analyses he was unable to find any trace of arsenic in the liver, spleen, muscle, stomach, cellular tissue, lungs, salivary glands, kidneys, suprarenal capsules, testicles, intestines, urine and blood of the animals examined[3]. Many analysts, following Gautier, found arsenic in human organs, while others were unable to find any trace of it. Bertrand[4] did not examine human organs, but, from his results on the tissues of pigs, calves, seal, and a variety of salt-water fish, reptiles, crustaceans, and molluscs, he goes even further than Gautier in assuming that arsenic is an essential constituent of protoplasm. Segale[5] found arsenic in the tissues of guinea-pigs, dogs, hens, and sparrows, in almost all organs of new-born human infants and foeti, and in menstrual blood. On the other hand Hödlmoser[1], Ziemke[2], Cerny[3], Bloemendal[4] and others either found arsenic absent or, if occasionally present, in faint traces only. They do not believe that this inconstant trace justifies the assumption that arsenic is normal to man.

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[1] People *v.* Zalimas, 319 Ill. 186.

[2] Bull. de l'Acad. de Méd., 1899, 3S., **42,** 561; C. R. Acad. des Sci., 1899, **129,** 189 & 929.

[3] Bull. de l'Acad. de Méd., 1900, 3S., **43,** 116; C. R. Acad. des Sci., 1900, **130,** 284; 1900, **131,** 361; 1902, **134,** 1394; 1902, **135,** 812; 1903, **137,** 295; 1920, **170,** 261.

[4] C. R. Acad. des Sci., 1902, **134,** 1434; 1902, **135,** 809; 1903, **136,** 1083; 1903, **137,** 266; Ann. de l'Instit., Pasteur, 1903, **17,** 1.

[5] Ztschr. f. physiol. Chem., 1904, **42,** 175.

As our previous discussion has shown that arsenic is almost constantly present in the air, soil, some natural waters, many vegetables, fruits, and meats, it is not surprising that arsenic may be found in the organs of individuals, who have not been under any arsenical form of treatment. As an evidence of this ingestion of arsenic, one may take its excretion in the urine. Thus, Putnam[5] states that of 48 samples of urine collected at random from the outpatients at the Massachusetts General Hospital 21 were found to contain traces of arsenic; Hills[6] examined 260 samples from 180 patients and found arsenic in 135; while Bang[7] found arsenic in 25 normal urines, in some cases as high as 0.5 mg. in daily amount, the greatest quantity being found after a fish diet. In the work of Fordyce, Rosen and Myers[8], it is shown that "as a result of the examination of the blood, urine, hair and milk from about 200 subjects we can conservatively state that arsenic is found 'normally' in a large number of persons, depending on the character of their food, drink, medication and environment." It is clear from the experiments of these workers that the so-called "normal" arsenic is derived from the many extraneous sources of arsenic to which we are all subject. Billeter and Marfurt[9] found arsenic in all tissues examined, the amount in each organ increasing from birth to adult life. They believe that an adult would have in his tissues an amount of arsenic averaging about 0.1 mg. per kilo of weight. Myers and Cornwall[10], in the analyses of a large series of individuals taken at random, showed that arsenic was, in most cases, a normal constituent of the urine, the presence of 0.40 mg. of arsenic per 100 grams of dried specimen being regarded as a normal value for urine, while the value for blood should not exceed 0.30 mg. per 100 gms. of dried specimen. The livers of individuals dying from natural diseases showed amounts of arsenic varying from traces to 0.174 mg. per 100 gms. of dried material, while the kidney content ranged from a trace to 1.282 mg. These workers sound the following warning: "Without establishing the presence or absence of syphilis and without a clear-cut statement as to whether the individual may have been treated with arsenic in the form of salvarsan, it will be difficult to state whether arsenical poisoning has been the cause of death, unless amounts in excess of those cited as normal values are found."

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[1] Ztschr. f. physiol. Cem., 1900, **33**, 329.

[2] Vrtljschr. f. ger. Med., 1902, **23**, 51.

[3] Ztschr. f. physiol. Chem., 1902, **34**, 408.

[4] Dissert., Leyden, 1908.

[5] Boston Med. & Surg. Jour., 1890, **122**, 421.

[6] Boston Med. & Surg. Jour., 1894, **131**, 453.

[7] Schweiz. Apoth. Ztg., 1917, **55**, 393. See, also, Petrén, Acta Med. Scand., 1923, **58**, 217.

[8] Arch. Int. Med., 1923, **31**, 739.

[9] Helvetica Chim. Acta, 1923, **6**, 780. Abs. in Chem. Abs., 1924, **18**, 404.

[10] Amer. Jour. Syph., 1925, **9**, 647.

While this question of "normal" arsenic may be of some interest to the biochemist, it does not, as stated by Witthaus, concern the toxicologist, to whom it is immaterial whether arsenic found in these minute quantities with great frequency in certain organs, not usually submitted to analysis in forensic cases, is normal or of fortuitous origin. Much the same idea is expressed by Kunkel[1], when he says: "The so-called normal arsenic, if there is such a thing, does not affect the results of forensic chemistry, because the so-called normal quantities are so exceedingly small (0.01 or even 0.001 mg. in an organ) that the quantities necessary to furnish a satisfactory forensic proof, which are a hundred or even a thousand times greater, must be regarded as an entirely different and much higher order of magnitude."

Arsenic Eating.—Tolerance to Arsenic.—From continued use of arsenic individuals appear to be able to establish more or less of a tolerance to this poison, so that, by carefully increasing the dose at somewhat long intervals, they may accustom themselves to take amounts of arsenic which would produce toxic symptoms in those unaccustomed to its use. From the time of the publication of the papers of Tschudi[2], in which he describes 3 cases of arsenophagia, there has been considerable discussion of this habit of arsenic eating, which appears to be somewhat common in Styria, Hungary and in parts of India. Thus, Taylor[3] states that "There is no proof that a human being has ever accustomed himself by habit, to take such substances as arsenic or corrosive sublimate in doses that would prove fatal to the generality of adults"; while Christison[4] and Kesteven[5] were very strong in their condemnation of the doctrine of inducing tolerance to arsenic. However, personal observations of many writers have shown that arsenic is regularly eaten in Styria and in others parts of the world in quantities usually considered sufficient to produce death rapidly. Thus, Schäfer[6] reported the case of a man of 30 years, who took, in his presence, 4½ grains of white arsenic and on the succeeding day 5½ grains, and who left quite well on the succeeding day without having manifested any arsenical symptom while under observation for the 3 days, although the urine contained arsenic; Parker[7] reports the case of an English arsenic eater whose daily dose was between 2 and 3 grains of white arsenic, who had taken it for 4 years and finally died of an overdose taken with suicidal intent; La Rue[8] published his observation of an arsenophagist in Quebec, who took in his presence 4 grains of white arsenic without suffering any inconvenience during two days of observation; Stewart[1] cites the case of a student in Dublin, who, of his own knowledge, was accustomed to eat pieces of white arsenic of about 3 or 4 grains without apparent harm. Hausmann states that the highest certainly determined dose taken by an arsenophagist was 0.42 gram (6½ grains) of arsenic trioxide in substance.[2]

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[1] Ztschr. f. physiol. Chem., 1905, **44**, 511.

[2] Wien. med. Wchnschr., 1851, **1**, 454; 1853, **3**, 8.

[3] *On Poisons*, 3rd Amer. Ed., 1875, p. 68.

[4] Edinb. Med. Jour., 1855–56, **2**, 709.

[5] Assoc. Med. Jour., 1856, **2**, 721, 757 and 808.

[6] Sitzb. d. k. k. Akad. d. Wissensch. zu Wien, 1857, **25**, 489.

[7] Edinb. Med. Jour., 1864, **10**, 116.

[8] Boston Med. & Surg. Jour., 1866, **74**, 439.

The tolerance established by the arsenic eaters is a limited one, as an overdose has caused death in several instances. Providing the arsenophagist maintains his dose within the limits for which tolerance has been established, he never suffers the symptoms of chronic arsenical poisoning, but may be subject to a peculiar hoarseness and catarrh of the respiratory tract. If the use of the arsenic be suddenly stopped, these persons suffer from discomfort, weakness and trembling, which immediately disappear on taking arsenic.

The reason for this apparent tolerance for arsenic is uncertain. Cloetta[3] attributes a degree of developed tolerance to a diminished absorption owing to changes in the alimentary mucosa making it less permeable to arsenic trioxide. Joachimoglu[4], while somewhat skeptical toward the theory of perfect tolerance, believes that in persistent feeding with white arsenic there is a gradual recovery of the mucosa from the catarrhal condition first induced, so that it becomes more resistant to the irritant as well as less absorbent of the rather insoluble poison. Schwartze[5] shows that the toxicity of the different preparations of arsenous oxide varies according to the coarseness or fineness of their subdivision, so that the question of absorption and resulting tolerance may depend on varying solubility. Schwartze and Munch[6] were unable to habituate the cat to white arsenic fed in increasing doses at suitable intervals and believe that this failure is a fair criterion of the improbability of developing any noteworthy systemic or gastro-intestinal habituation to arsenic trioxide by feeding. Issekutz and Végh[7] show that, if arsenous acid in solution is administered to an animal rendered tolerant by the administration of the compound in its solid form, absorption through the intestinal wall is not inhibited and the dog will succumb to the intoxication, although it would not have shown the slightest symptoms, had the substance in many times the fluid dose been given in the solid form. These workers find that dogs cannot be rendered tolerant to solutions of arsenic trioxide and believe that the development of tolerance to the solid form is not primarily due to an acquired immunity of the intestinal wall but that the arsenic is not absorbed simply because it is not dissolved.

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[1] "Trials for Murder by Poisoning", p. 380. Cited by Glaister, *Medical Jurisprudence and Toxicology*, 4th Ed., 1921, p. 639.

[2] Arch. int. de ph. et de thér., 1903, **11**, 483.

[3] Arch. f. exper. Path. u. Pharm., 1906, **54**, 196.

[4] Arch. f. exper. Path. u. Pharm., 1916, **79**, 419.

[5] Jour. Pharm. and Exp. Therap., 1922, **19**, 258; Ibid., **20**, 181.

[6] Ibid., 1926, **28**, 351.

[7] Arch. f. exp. Path. u. Pharm., 1926, **114**, 206.

In trials for arsenical poisoning the defense has occasionally advanced the theory of arsenic eating to explain the presence of arsenic in the body, or has broached the use of arsenic as a cosmetic to explain the purchase of the arsenical preparation. It is stated that Tschudi's publication was prompted "by the outcome of a trial for murder by arsenic in which the defendant was acquitted, the defense having set up the theory that the deceased was an arsenic eater." In the case of Reg. *v.* Wooler[1] the theory of arsenic eating was contemplated by the defense but was later abandoned. In the Madeleine Smith case[2], who was accused of poisoning L'Angelier with arsenic, the purchase of arsenic was accounted for by her claim that she had bought arsenic on various occasions and had used all of it as a cosmetic, applying it to her face, neck, and arms in aqueous suspension. In the case of the People *v.* Sarah Harrington[3] it was proved that the deceased had for years used arsenic as a medicine for his horses and had taken it himself. In the famous Maybrick case[4] it was not only alleged that Mr. Maybrick (the deceased) was in the habit of using arsenic himself, but Mrs. Maybrick attempted to account for her purchase of arsenic on the basis of using it as a cosmetic.

Absorption—Distribution—Elimination.—Arsenic may be absorbed and taken up by the blood, when administered or applied in many different ways. While the oral route is the usual one and the one that most often arises in toxicological work, yet arsenic has proven fatal when given per rectum as an enema[5]; when it has been applied to the vagina[6]; when inhaled in tobacco smoke[7]; when absorbed from the unbroken skin[8]; when applied in the form of pastes for the treatment of cancer[9]; and when given in other ways.

When arsenic is taken in the solid form on an empty stomach, its absorption depends, to a great extent, upon the fineness of the particles, the solution of the crystals being more rapid in the fluids of the stomach the finer the powder. If food be present in the stomach, or is taken along with the arsenic, the rapidity of absorption is, of course, slower than if the stomach be empty. If the arsenic be taken in actual solution, absorption probably begins immediately and symptoms will appear much sooner than when it is ingested in the solid form. The arsenic, under these latter conditions, makes its appearance in the blood in a few minutes, and, in consequence, the tissues, especially the liver, kidneys and spleen, retain appreciable amounts of arsenic, and some of the absorbed arsenic will be promptly excreted by the kidneys. That the absorbed arsenic disappears very quickly from the blood stream is shown by the experiments of Fordyce, Rosen and Myers[1], which indicate that, following intravenous injection of salvarsan and neo-salvarsan, the blood taken *immediately* after the completion of the injection contains only 40 per cent. of the arsenic injected in the form of salvarsan while 60 per cent. is localized outside of the blood stream, and, in the case of neo-salvarsan, only 37.9 per cent. of the arsenic is in the blood stream, the arsenic equilibrium gradually becoming lower at later intervals up to one day.

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[1] Durham Winter Assizes, 1855. This is the first English case in which this plea was considered.

[2] Edinburg Court of Justiciary, 1857.

[3] Tried in Delaware County, New York in 1861. See Porter, Trans. Med. Soc. N. Y., 1862, p. 155.

[4] Tried at Liverpool Assizes, 1889. See Carter, Lancet, 1889, **1**, 1268; 1889, **2**, 506. Also Macdougall, "The Maybrick Case", 1891.

[5] See Fodéré, *Traité de médecine legale*, 1813, **4**, 266; People *v.* McCraney, 6 Harris C. R., 49.

[6] See Edling, Deutsche Klin., 1873, **41**, 391; Haberda, Wien, klin. Wchnschr., 1897, **10**, 201.

[7] See Schlegel, Jour. d. prakt. Heilk., 1827, **64**, 13.

[8] Taylor, Guy's Hosp. Reprs., 1864, 3s., **10**, 220; Tidy, Lancet, 1878, **2**, 250; Riedel, Vrtljschr. f. ger. Med., 1899, 3F., **17**, 49.

[9] Graham, Glasg. Med. Jour., 1868–69, **1**, 56; Cameron, Brit. Med. Jour., 1890, **2**, 203.

Just how long a time must elapse before all of the ingested arsenic will find its way out of the stomach, either by absorption or excretion, will depend upon the rapidity of absorption and the amount ingested. In a case reported by Smith[2], a nursing infant died on the second day, poisoned by the milk of the mother to whom arsenic had been criminally administered, the analysis of the liver showing the presence of arsenic while the fluid in the stomach showed no trace of arsenic. Such a case must be regarded as somewhat exceptional and would seem to indicate that arsenic in a readily absorbable form may pass out of the stomach in at least two days, but whether or not it was present in the stomach tissues was not determined. It is, rather, the rule to find some trace of arsenic in the stomach contents or tissues for longer periods than the above, but it is undoubtedly possible for all of it to be absorbed or ejected by the violent vomiting in some cases. It is to be said, however, that the arsenic found in the stomach has not been the cause of death, as a true poison must act after absorption and not by its mere local irritant effect. Hence, it follows that this poison must be shown to be present in organs other than the stomach, if one is to draw the conclusion that death is due to arsenical poisoning. It does not seem probable that one would find arsenic in the stomach, except possibly in mere traces, and not be able to detect it, also, in the other organs, especially in the liver, although two such cases[3] have been reported in the literature.

The *distribution* of the arsenic in the tissues of the body will depend, to a great extent, upon the interval between the taking of the toxic dose and the death of the individual. In the rapidly fatal cases, the stomach and its contents may show relatively larger amounts of arsenic than will the other organs, as there has not been sufficient time for much of the poison to be absorbed. However, if the vomiting has been excessive, a large part of the ingested arsenic may be lost by this procedure, although there are some reported cases in which considerable arsenic has remained in the stomach in spite of almost constant vomiting for several days. It is almost certain that there will be more arsenic found in the stomach if the poison be taken in the solid form than if it be ingested in solution, as the former has a tendency to attach itself to the mucosa and to resist the repeated efforts to eject it in the vomitus.

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[1] Amer. Jour. Syph., 1923, **7,** 225; Ibid., 1924, **8,** 34.

[2] Buffalo Med. Jour., 1852–53, **8,** 730.

[3] See Casper-Liman, *Handbuch der gerichtlichen Medicin,* 8te. Aufl., 1889, **2,** 412; and Pinkham, Trans. Mass. Med.-Leg. Soc., 1878, **1,** 43.

In regard to the amount of absorbed arsenic, it is to be said that, as a rule, the liver, kidneys and spleen contain a greater proportion of the arsenic than an equal weight of muscle, brain, or other tissues, especially in the cases which are relatively rapid; while, if the death be delayed for some days, the tendency is toward a more nearly equal distribution of the arsenic in the different organs. However, there is no definite rule as to the comparative weights of arsenic that may be found in the different organs. While the amount of arsenic in the alimentary tract is usually greater, the shorter the duration of the poisoning, yet there are many cases in which this condition does not prevail[1]. Further, the liver and kidneys may vary in their relative amounts of arsenic in different cases. Thus, in one case[2] 100 grams of kidney contained 3 times as much arsenic as the same quantity of liver, while in another case[3] the liver tissue contained 33 times as much arsenic as the same quantity of kidney tissue. While several series of analyses have been made of the distribution of arsenic in fatal cases, we cite, as a fair example of the conditions ordinarily prevailing, the cases of McNally[4] as follows: In case 1 death occurred 4½ hours after taking an unknown quantity of some form of arsenic, the autopsy being made on the exhumed body 9 days after death. In 100 grams of tissue, the following amounts of arsenic (as As.) were found: stomach walls, 0.0249 gm.; stomach contents, 0.8926 gm.; liver, 0.0144 gm.; small intestine, 0.0134 gm.; large intestine, 0.0262 gm.; left kidney, 0.0093 gm.; right kidney, 0.0082 gm.; heart, 0.0065 gm.; pancreas, 0.0095 gm.; lung, 0.0021 gm.; gall-bladder, 0.0042 gm.; esophagus, 0.017 gm.; and brain, 0.0002 gm. In McNally's second case, a chronic one in which death occurred 3 weeks after the first dose of arsenic and 10 days after the second dose, the findings were as follows: In 100 grams of tissue the spinal cord contained 0.0011 gm. of arsenic (as As.); blood, 0.0005 gm.; stomach walls, 0.0005 gm.; stomach contents, 0.0005 gm.; kidney, 0.0016 gm.; spleen, 0.0013 gm.; liver, 0.0013 gm.; and urine, 0.0017 gm.

Outside of the stomach and intestines, the liver is, probably, the most important organ for toxicological examination, owing to the fact that the arsenic is retained in it to a greater extent than elsewhere. Although the statement is made[1] that "The total quantity of arsenic trioxide in the liver at death probably never exceeds 0.2 gm. (3 grains), if indeed it ever reaches that amount", yet there are several cases in the literature in which more than 3 grains have been found. Thus, Bingley[2] finds 4.15 grains in "not quite half of the liver"; Barker[3] reported a case in which the liver contained 5 grains; Blarez and Denigès[4] reported 3 cases showing respectively 217, 258, and 330 mg. of arsenic per kilo of liver, which represents, on the basis of a normal weight of 1450 grams for the liver, 0.315 gm. (4.86 grains), 0.374 gm. (5.77 grains), and 0.478 gm. (7.37 grains) respectively; while Loevenhart[5] in an unpublished analysis in a case of homicidal poisoning found 0.27 gram (4.17 grains) in 1010 grams of the liver submitted to him for examination. On the basis of a normal liver weight of 1450 grams, this would represent a total As_2O_3 content of 0.388 gram (6 grains).[6] While these cases would seem to indicate that the point of saturation of the liver with arsenic trioxide is, occasionally at least, higher than the 3 grains ordinarily stated, yet it must be granted that the usual finding is less than 3 grains rather than above this figure.

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[1] See Lesser, Vrtljschr. f. ger. Med., 3f., 1897, **14,** 287; 1898, **15,** 27 and 261; **16,** 60; Schönberg, Deutsche Ztschr. f. d. ges. gerichtl. Med., 1929, **13,** 111.

[2] Lesser, *Atlas der gerichtlichen Medizin,* 1884, **1,** 90.

[3] Chittenden and Smith, Med.-Leg. Jour., 1885, **3,** 46.

[4] Jour. Amer. Chem. Soc., 1917, **39,** 826. See, also, Willcox, Brit. Med. Jour., 1922, **2,** 118.

While arsenic may usually be found in the soft tissues submitted for examination, providing death has not been delayed for some time, yet there are undoubted cases in which no arsenic has been found in any of such tissues after a period of 14 days or even less. Under such conditions arsenic may be found in the bones and hair, which should be examined in doubtful cases. Brouardel[7] states in this connection that "arsenic accumulates very sensibly in the *spongy tissue* of bones and becomes fixed in such manner that its presence can be detected, in the bones of the skull or vertebrae particularly, some time after every trace has disappeared from these organs, such as the liver, in which it is localized in greater amount." It would appear that this localization in the bones is less marked and the elimination more rapid when arsenic is absorbed in quantities sufficient to cause rapid symptoms of poisoning, a point which has been brought out by Chittenden[8] in connection with the differentiation between acute and chronic arsenic poisoning, the bones tending to retain arsenic in the chronic cases while, in the acute cases, arsenic may not be found in the bones.

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[1] Witthaus, *Toxicology,* 1911, p. 532.

[2] Lancet, 1864, **1**, 697.

[3] Cited by Wharton and Stillé, *Medical Jurisprudence,* 1884, **2**, 563.

[4] Compt. rend. Soc. de Biol., 1905, **58**, 279.

[5] Personal communication: Case of Wisconsin *v.* Lottie Gardinier.

[6] This case is peculiar in that Fred Gardinier, the deceased, was up and about all the time during his fatal poisoning and there was no evidence of vomiting at any time during his illness. He died suddenly, when he went out to milk the cows.

[7] Ann. d'Hyg., 1889, 3s., **31**, 486; Bull. Acad. de Méd., 1889, 2s., **22**, 4 and 53.

[8] Med.-Leg. Jour., 1884, **2**, 244.

In connection with the distribution of arsenic in the tissues in cases of poisoning, it is interesting to find that, when a pregnant woman dies from the effects of arsenic, this poison is found in the foetus and its coverings but not in the amniotic fluid[1]. Underhill and Amatruda[2] have shown in their animal experiments that arsenic is detected in small traces in the fetal tissues after the intravenous injection of neo-arsphenamine into the maternal circulation and that the arsenic is stored in the maternal liver and placenta.

Elimination of arsenic probably begins very soon after its ingestion, the rate depending upon the rapidity of its absorption. The elimination takes place largely through the feces and urine, although the skin and hair[3] may play a role. It is to be expected that some arsenic might be excreted almost as soon as it has been absorbed into the blood. Thus, Mann[4] states that arsenic may be detected in the urine in ½ hour after administration of 5 drops of Fowler's solution, while Husemann[5] asserts that it appears in the urine often in 5 to 6 hours and with potassium arsenite in an hour. In the experiments of Fordyce, Rosen and Myers[6], in which the rapidity and continuation of excretion of arsenic following intravenous injection of salvarsan, neosalvarsan, silver-salvarsan and tryparsamide was studied, arsenic was found in the urine in 5 minutes after the injection in 10 cases, the amounts being variable and a decline in the amount being observed over a period of 1 week.

The elimination of arsenic by the urine appears to vary, both in amount and duration of excretion, depending upon the manner of administration, that is whether it be given in a single large dose or in repeated small doses. If a large single dose be taken, the elimination begins promptly and ordinarily continues, in decreasing amounts, for 4 to 5 days[7], although Dutcher and Steel[8] in their animal experiments find that a single non-poisonous dose is eliminated in about 15 days, and Maclagan[9] reports arsenic in the urine 21 days after its administration, while Wood[10] detected arsenic in the urine 93 days after a single large dose.

If the arsenic be administered in small repeated doses, the type of elimination is different from that mentioned above, as long periods of excretion are the rule and shorter ones the exception. Thus, Gaillard[11] reports the detection of arsenic 40 days after cessation of arsenical treatment; Wood[1] in 59 days in one case and in 83 days in another; Almqvist and Welander[2] up to 7 months; Shepherd[3] in 111 days after a course of 7 injections of neo-salvarsan; and Watson[4] in 15 months after a course of 10 injections of neo-salvarsan. It should be mentioned that the failure to detect arsenic in the urine cannot be taken as absolute proof that elimination is complete, as arsenic may not be found in some specimens and will be detected in others. Thus, in the case reported by Maclagan[5], arsenic was not found in the urine passed on the twelfth day after ingestion of 8 grams of arsenous oxide, but was found in the urine on the 16th and 21st days. Further, the excretory action of the kidney may be diminished to such an extent that the urine no longer contains detectable amounts of arsenic, and yet after death the poison may be found in the tissues.

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[1] See Bischoff, in *Atlas der gerichtlichen Medizin,* by Lesser, 1884, **1**, 89.

[2] Jour. Amer. Med. Assoc., 1923, **81**, 2009.

[3] Althausen and Gunther, Jour. Amer. Med. Assoc., 1929, **92**, 2002.

[4] Med.-Chir. Trans., 1901, **84**, 435.

[5] *Handbuch der Toxikologie,* 1862, p. 823.

[6] Amer. Jour. Syph., 1924, **8**, 619.

[7] See Rademacher, Richm. and Louisville Med. Jour., 1873, **15**, 383; Powell, Westm. Hosp. Rep., 1889, **5**, 215; and Severi, Jahresber. f. d. Thierch., 1893, **23**, 105.

[8] Jour. Amer. Chem. Soc., 1914, **36**, 770.

[9] London and Edinburgh Monthly Jour. Med. Soc., 1852, **14**, 132.

[10] Boston Med. and Surg. Jour., 1893, **128**, 414.

[11] Bull. Soc. méd.-lég., Paris, 1873–74, **3**, 249.

While the urine is an important channel of elimination of arsenic, it is probable that a larger proportion of the ingested poison is eliminated by the feces and, also, that arsenic may be found in the feces and not in the urine. Thus Sonnenschein[6] reports a case of poisoning by repeated doses of extract of fly papers in which arsenic was found in the feces but none in the urine. While there is no question of the excretion of arsenic in the feces, few studies have been made on the quantitative excretion by this route. Fraenkel-Heiden and Navassart[7] find that the quantity of arsenic excreted through the intestine, following either intramuscular or intravenous administration of salvarsan, is from 2 to 10 times greater than that passing through the kidney; Marthens[8] states, "Of the total quantity injected about 60 per cent of arsenic is lost in the excreta during seven days. From 10–15 per cent of the injected arsenic appears in the urine during six days but a much larger elimination takes place through the feces"; while Clausen and Jeans[9] conclude that arsenic is excreted 5 times as rapidly in the stools as in the urine; and Underhill and Davis[10] state, "In a series of injections the total percentage of arsenic excreted in the feces is larger than in the urine, being as high as 53.76 per cent in one week."

An interesting method of excretion of arsenic is through the horny epithelial scales exfoliated by patients with arsenical keratosis. Mann[11] was able to extract from 10 grams of these scales 0.8 mg. of arsenic, while

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[1] *Loc. cit.*

[2] Cited by Heffter, Ergebnisse d. Physiol., 1903, **2,** 115, who himself reports arsenic in the urine 3 weeks after taking Royat water for 14 days.

[3] Lancet, 1921, **2,** 1273.

[4] Ibid., 1922, **1,** 815.

[5] London and Edinburgh Monthly Jour. Med. Soc., 1852, **14,** 132. See, also, Ritter, Rev. med. de l'Est, 1878, **9,** 257.

[6] *Handbuch der gerichtlichen Chemie,* 1869, p. 120.

[7] Ztschr. f. exp. Path. u. Therap., 1913, **13,** 531.

[8] Ohio State Med. Jour., 1922, **18,** 13.

[9] Amer. Jour. Syph., 1922, **6,** 556.

[10] Arch. Dermat. and Syph., 1922, **5,** 40.

[11] Lancet, 1901, **2,** 385.

Fordyce, Rosen and Myers[1] found arsenic in the desquamating scales following administration of organic arsenicals, in amounts varying from 0.123 mg. to 315.9 mg. Osborne[2] demonstrated that arsenic becomes localized in the epidermis, subpapillary layer, and other ectodermal tissues following administration of such arsenicals as Fowler's and Donovan's solutions, while after administration of the arsphenamines keratoses and pigmentation appear rarely. Later Osborne[3] showed that there was a difference in localization of arsenic according to the valency of the compound. Thus, the trivalent compounds seem to have a special affinity for the vascular structures, such as the small arterioles and capillaries below the papillae of the cutaneous tissues, while the pentavalent arsenicals seem to be attracted by the ectodermal structures and, hence, more readily produce pigmentation, keratoses, mild dermatitis, wrist drop, and optic atrophy, while the trivalent products produce severe dermatitis, hemorrhagic encephalitis, and purpura. Althausen and Gunther[4] have shown that such epidermal structures as the hair eliminate arsenic to a large extent. These workers find that, while arsenic does not appear rapidly in the hair (being demonstrated at the earliest 5 days after the beginning of the poisoning), yet the amount present in the hair per unit of weight surpasses that in any other tissue, and is retained much longer than in other tissues.

Although arsenic may be detected in traces in the urine, feces, and hair for some time, in occasional cases, elimination of the arsenic from the tissues, following a single large dose, is practically complete in about 2 weeks. Yet, in those cases in which arsenic is found in the urine, we must assume its presence in the tissues also. We have, of course, no means of knowing how much arsenic is present in the tissues or of determining its distribution unless death occurs, so that the above statement applies only to recorded cases of death. Probably, the longest duration of an acute fatal case, in which arsenic has been found in the tissues, is the one reported by Chittenden[5], in which death followed in 14 days after a single dose.

Symptoms of Acute Poisoning.—The first symptoms of arsenical poisoning usually do not appear before ½ to 1 hour after the poison is swallowed. However, fatal cases have been reported in which the manifestations came on "immediately"[6], one in 8 minutes[7], and others in a "few minutes"[1]. In the "mass poisoning", which occurred at a prominent Club in Chicago in 1916, over 200 were showing the symptoms of gastro-intestinal irritation before all of the people at the banquet had been served with the soup in which the arsenic was contained. While it is a general rule that the symptoms appear sooner when the arsenic is given in solution than when it is ingested in solid form, yet in occasional cases the manifestations may appear rapidly when the poison is taken in food, as in the case of Shaw and Lofthouse Case cited above. Further, rapidity of symptoms does not always depend upon the size of the dose, as some cases show prompt disturbances from small doses, while in others the symptoms have been somewhat delayed after relatively large amounts. Just as some cases show rapid development of symptoms, others show a delayed interval, as cases are recorded in which the interval has been prolonged for 5 hours[2], six hours[3], eight hours[4], nine hours[5], ten hours[6], and 16 hours[7]. The delay in appearance of symptoms depends upon the form in which the poison is ingested, on the presence of food in the stomach, and on certain influences which modify the action of the poison, as, for instance, when taken in conjunction with opium[8], when taken by a person under the influence of alcohol[9], and when the person goes to sleep after taking the arsenic[10]. It is interesting to note that, when the interval elapsing between the taking of the poison and the manifestation of the symptoms is either short or prolonged, the poisoning is usually severe and its duration short. Thus, Witthaus[11] states that in ten fatal cases in which the interval was less than 20 minutes the patients expired in periods ranging from "immediately" to 24 hours, while of 29 cases, in which symptoms were late in appearing, 21 terminated fatally and of these 13 in less than 24 hours.

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[1] Amer. Jour. Syph., 1923, **7,** 209.

[2] Arch. Dermat. and Syph., 1925, **12,** 773.

[3] Ibid., 1928, **18,** 37.

[4] Jour. Amer. Med. Assoc., 1929, **92,** 2002.

[5] Med.-Leg. Jour., N. Y., 1884, **2,** 243.

[6] See Iliff, Lancet, 1845, **2,** 432; Taylor, Guy's Hosp. Rep., 1851–52, 2s., **7,** 203; Shaw, Lancet, 1879, **1,** 699; Shepard, Trans. South Carol., Med. Assoc., 1880, **30,** 21; Taylor, *On Poisons*, 3rd Amer. Ed., 1875, p. 288 (Lofthouse Case tried at the York Lent Assizes in 1835); Elwell, *Malpractice and Evidence*, 1860, p. 504 (Case of State *v.* Sager).

[7] Christison, *A Treatise on Poisons*, 1st Amer. Ed., 1845, p. 235.

The clinical picture of arsenical poisoning is, by no means, always the same, departures from what are called the typical forms being frequent and no symptoms being regarded as absolutely characteristic of this intoxication. The interpretation of a case of suspected arsenical poisoning should rest on both the chemical and post-mortem findings, as many anomalous cases will be found in which somewhat typical clinical signs will be present, without the usual autopsy findings, while other cases will present themselves in which the clinical signs are vague and confusing while the postmortem appearances will be found to be typical of arsenical poisoning. In such cases, the chemical examination of the tissues will have to solve the question involved. The fact that many cases show a delay in the appearance of symptoms is evidence that the toxic action of arsenic is really a result of action after absorption and not a consequence of direct gastro-intestinal irritation. Further, it should be mentioned that, when many individuals are poisoned at the same time and apparently under the same conditions as to dosage, form of poison taken and condition of the stomach, the symptoms manifested by the victims are, by no means, the same in all cases, some showing one type and others varying symptoms[1]. In a general way the symptoms of acute arsenical poisoning may be divided into two groups: the one of most frequent occurrence being characterized by an intense gastro-enteritis, and styled by von Hasselt *Arsenicismus gastro-intestinalis;* while the second type, which is much less frequent, is marked by symptoms referable to a severe cerebro-spinal action and is styled *Arsenicismus cerebrospinalis.*

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[1] See Paterson, Edinb. Med. Jour., 1857, 3, 397; Editorial, Prov. Med. and Surg. Jour., 1841, **3**, 257; and Horsford, Phila. Med. and Surg. Reptr., 1867, **16**, 45.

[2] See Taylor, Guy's Hosp. Repts., 1865, 3s. **11**, 277; and Thomson, Lancet, 1853, **2**, 480.

[3] See Fox, Lancet, 1848, **2**, 503; and Virchow, Arch. f. Path. Anat., 1869, **47**, 524.

[4] Tonnelier, Jour. de med., chir., et pharm., 1802, **4**, 15. Cited by Flandin, Traité des Poisons, 1846, **1**, 530.

[5] Ryan, Lancet, 1851, **1**, 410.

[6] Taylor, *On Poisons*, 3rd Amer. Ed., 1875, p. 289.

[7] Hartshorne, Medical Examiner, 1855, p. 707.

[8] Clegg, Med. Times, 1849, **19**, 26; Joachimoglu, Klin. Wchnschr., 1922, **1**, 169.

[9] Gérard, Rev. méd., 1822, **7**, 105; Ward, Edinb. Med. and Surg. Jour., 1830, **33**, 61; Ryan, Lancet, 1851, **1**, 410; and Bryant, Lancet, 1862, **2**, 299.

[10] See Christison, *A Treatise on Poisons*, 1st. Amer. Ed., 1845, p. 235 and 236 (Case of Rex. *v.* Mary Smith); and Devergie, Médecine Légale, 3éme ed., 1852, **3**, 519.

[11] *Toxicology*, 1911, p. 447 and 452.

Gastro-enteric Type.—Soon after swallowing the toxic dose, the time varying as we have seen, the patient complains of a burning or irritating feeling in the throat and esophagus accompanied by a sensation of faintness, depression and nausea. Soon, thereafter, there is intense pain in the stomach, which is burning in character, is frequently characterized by the patient as "like a red-hot coal in the stomach", increases rapidly in severity and is aggravated by pressure. The mouth is dry and parched and intense thirst is complained of. Retching and vomiting appear early in the attack, increase in severity and become almost persistent. The vomitus at first consists of the food residue, but later becomes thin and watery, then mucoid, and later brownish from the presence of bile or tinged with blood. The color of the vomitus may give some evidence of the presence of arsenic, as, for instance, green from Paris green, yellow from arsenic sulphide, or black from the lampblack occasionally mixed with arsenic in "Rough on Rats." Shortly after the vomiting begins, severe purging is observed, the stools being at first dark-colored and very offensive, but soon becoming thin and watery like the "rice-water" stools of cholera, and tenesmus may be marked. The urine may be scanty or even suppressed, and may contain albumin, blood and casts as an evidence of a severe parenchymatous nephritis. The skin is cool and clammy. The face is at first pale but later becomes cyanotic, while slight jaundice may be noticed on the skin and sclera. The patient now complains of headache, cramps in the calves of the legs and other muscles, and general weakness. The pulse is small, feeble, frequent, and irregular, while the respiration is only slightly interfered with. The patient gradually becomes greatly prostrated, there may be convulsive movements of various groups of muscles, and complete collapse and death end the picture.

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[1] See Taylor, *On Poisons*, 3rd Amer. Ed., 1875, p. 291 for poisoning of 340 children with milk, each child receiving about 1 grain of arsenic; Morley, Virchow's Jahresber., 1876, **1**, 362, for poisoning of 15 persons with arsenic-containing pudding; and Lawson, Jackson and Cattanach, Jour. Amer. Med. Assoc., 1925, **85**, 24, for a report of 28 cases of poisoning, 13 of which were fatal, from arsenic-containing cider, in which there was a wide variety of symptoms.

Cerebrospinal Type.—In this type the signs of gastro-enteritis are slight or wholly absent. There may be slight pain, nausea and a few intermittent attacks of vomiting, but, as a rule, such symptoms may be almost unnoticed. The attack begins with vertigo and headache, spasms of the muscles of the extremities, stupor, delirium, and disturbances of sensation. In a short time, usually in a few hours, general paralysis, collapse and death occur. In some cases, the symptoms of both types of arsenical poisoning may be combined. Just what determines the type of arsenical poisoning is not known, but it seems reasonable to assume that whatever favors quick absorption of the poison, and, therefore, quick development of the symptoms, will tend to the appearance of the cerebrospinal type of arsenical poisoning.[1]

Subacute Form.—This is a mixed form of arsenical poisoning and usually follows the administration of small doses repeated at intervals, so that marked symptoms do not appear so quickly and are not as severe as in the true acute type. Sooner or later there is loss of appetite, fainting sensations, nausea, dry throat, thirst, retching, vague shooting pains in the stomach and bowels, followed by more or less violent vomiting and diarrhea, which lessen in intensity in 24 to 48 hours. The urine diminishes in quantity and shows evidence of nephritis and jaundice may appear as a sign of the hepatic disturbance. The eyes become suffused and the conjunctiva are injected, while varied types of skin eruptions may be noticed, especially erythematous and eczematous types with pigmentations and keratosis. Under proper treatment the acute symptoms may subside and some time later signs of peripheral neuritis will appear, causing numbness and tingling in the extremities, muscular pains, paralysis in the hands and feet followed by wasting of the muscles. In the more progressive cases, there is gradual weakness, the heart's action becomes weak and irregular, the respiration may become dyspneic, there may be delirium, stupor, and convulsions followed by death.

The sequence of symptoms in the above types of arsenical poisoning is usually continuous, although there may, occasionally, be remissions. It should be remembered that the symptoms mentioned in the acute and subacute types may not occur in their entirety in every case, as many cases are reported in which there was no thirst, no pain in the stomach, no vomiting, and no purging. While one or more of these symptoms are usually noted, yet some of them may be absent. In some of the cases, convulsions, when they have occurred at all, have been of the true tetanic rather than the usual clonic type, so that the symptoms may closely resemble those of strychnine poisoning and thus lead to confusion. Another point that should be mentioned is that, when arsenic is administered by parenteral routes, the symptoms shown are much the same as those when ingestion is by mouth, with the addition of purely local manifestations, although the gastrointestinal irritation is not so prompt in appearing.

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[1] See Hofmann-Haberda, *Lehrbuch der gerichtlichen Medizin*, 11te. Aufl., 1927, p. 837.

Chronic Form.—While arsenic is not to be regarded as a cumulative poison in the sense that repeated small doses may gradually accumulate in the system and suddenly produce symptoms of acute poisoning, yet the effects of small doses may gradually lead to symptoms which do, undoubtedly, indicate an exaggeration of the effects of arsenic and which are not directly the resultant of single large doses. Probably, the chronic effects are due to pushing the small doses beyond the limits of tolerance of the individual, although it must be admitted that chronic poisoning may follow acute cases, especially when death is delayed for some time.

The symptoms are usually ushered in by a feeling of general malaise, faintness and loss of appetite. There may be twinges of colic-like abdominal pain and mild gastric irritation may lead to sudden and copious vomiting. Constipation is more usual than diarrhea. There may be mild fever, the temperature rarely exceeding 103°. The eyelids become puffy, the face pale and waxy. There may be salivation with more or less stomatitis. The throat, nose, larynx and bronchial tubes may show a catarrhal affection, leading to hoarseness and huskiness of the voice, coryza, aphonia, cough and bloody expectoration. At the same time the eyes become suffused and there is considerable conjunctivitis. The hair becomes dry and may fall out, and the nails brittle and loose, while the skin may show a varying picture of such lesions, as erythema, eczema, pigmentation and keratosis[1]. Kraetzer[2] reports Raynaud's disease as associated with chronic arsenical retention. Ascites as a result of portal cirrhosis may be rather marked. At a varying interval after the beginning of symptoms, the patient complains of severe headache followed by signs of peripheral neuritis, such as a feeling of numbness in the legs and feet, with tingling, burning and prickling in the toes and fingers, which are followed eventually by total absence of normal sensation, or, in some cases, by severe pains and tenderness. Later motor disturbances may follow, but, in some cases, are slight or even absent. These may begin with muscular weakness, the foot being first affected, then the muscles of the calves and later those of the thigh; while in the upper extremity the paralysis begins with the small muscles of the hand and extends upwards. The muscles become atrophied and lose their faradic excitability entirely or at least partially, while the excitability to the galvanic current is usually retained to a more or less extent. The paralysis may extend until it is quite general and may last for many months, recovery being slow and generally incomplete. Death most frequently results from cardiac weakness as a result of fatty degeneration.

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[1] See Lawson, Jackson and Cattanach, Jour. Amer. Med. Assoc., 1925, **85**, 24; O'Leary, Snell, and Bannick, Ibid., 1928, **90**, 1856. Thirty per cent. of all cases of eczema studied by the N. Y. Skin and Cancer Hospital are said to be due to arsenic poisoning. See Myers and Cornwall, Amer. Jour. Syph., 1925, **9**, 647; Throne, Vom Dyrk, Marples, and Myers, N. Y. State Jour. Med., 1926, **26**, 843.

[2] Jour. Amer. Med. Assoc., 1930, **94**, 1035.

Fatal Dose.—The smallest fatal dose of arsenic, calculated as As_2O_3, is two grains as reported by Castle[1]. In this case a woman, who had recently aborted, committed suicide by taking ½ ounce of Fowler's solution (equal to 2 grains of arsenic trioxide) in divided doses over a period of 4 days. Letheby[2] reports the death of a healthy, robust girl of 19 years from a dose of about 2 ounces of fly-water containing 2½ grains of white arsenic. Fahrenhorst[3] records the death of a boy of 4 years from 4½ grains. Rouyer[4] found in his experiments on dogs that absorption of 0.0025 gram of As (0.0033 gram As_2O_3) per kilo (0.02376 grain per pound) sometimes, and of 0.003 gram of As (0.004 As_2O_3) per kilo (0.02772 grain per pound) always caused death. Making the usual allowance for body weight, this puts the fatal dose of arsenic trioxide for a man of 150 pounds at 0.22 to 0.26 gram (3.4 to 4 grains).[5] From a consideration of the cases cited and the experimental work of Rouyer, one is justified in the conclusion that 3 grains of absorbed arsenic would probably prove fatal to an average man, as is stated by practically all authorities on toxicology. However, Witthaus[6], while stating that he was unable to find "any record of the clearly established death of an adult from a single dose of less than 2 gm. (thirty grains) of arsenic in the solid form", practically admits that his opinion is the same as that of other toxicologists.[7]

While 3 grains of absorbed arsenic may be regarded as the probable minimum fatal dose of arsenic, it must be said that recovery has followed the taking of much larger doses. Thus Glaister[1] reports recovery following 15 grams (231 grains); Rademaker[2] from 30 grams (1 ounce); and Jackson[3] from 60 grams (2 ounces).

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[1] Prov. Med. and Surg. Jour., 1848, p. 347. See, also, Lachèse, Ann. d'Hyg., 1837, **17**, 334.

[2] Lancet, 1847, **1**, 44.

[3] Mag. f. d. ges. Heilk., 1823, **20**, 483.

[4] These de Nancy, 1875. See, also, Rouyer and Feltz, Gaz. d. hôp. de Paris, 1875–76, **1**, 962.

[5] These figures are slightly at variance with those usually quoted for the work of Rouyer. Dr. E. W. Schwartze called our attention, in connection with the revision of Peterson, Haines and Webster's Textbook, to the fact that Rouyer, through a typographical error had allowed the figures reported apparently to represent arsenic trioxide, when, in reality, it is clear from his thesis that the figures apply to arsenic as such.

[6] *Toxicology*, 1911, p. 439.

[7] On page 440 of his Toxicology, Witthaus states: "Our own opinion, clearly differentiated from our statements of fact, and based principally upon the occurrence of severe, non-fatal poisonings from doses of from one to twenty grains is that the minimum lethal dose for man is probably much below 30 grains, and possibly may be as low as 'three grains of absorbed arsenic' ". A little further on in this work (page 442) he states: "There are also numerous instances upon record, in which very severe poisoning has been caused in adults by doses as small as 0.065 gm. (one grain), and in children by even less quantities. And it may be conceded that in some of these cases death might have resulted had not the patients received suitable treatment."

Fatal Period.—Taylor[4] cites a case in which the interval before death was 20 minutes, but there seems to be some doubt whether or not the dose may not have been taken earlier than assumed. In the case reported by Iliff[5] death came "instantly", but it would seem that some cause other than arsenical poisoning must have been accountable for the sudden death. As a rule, when the symptoms appear suddenly, death usually occurs relatively soon. The usual duration of a fatal case is about 24 hours, although death has occurred in 1 hour[6] and in 2 hours[7], while Witthaus[8] states that he has collected from the literature (up to 1911) 53 cases, 3 of which died in 3 hours, 10 in 4 hours, 6 in 5 hours, 2 6 hours, 15 in 7 hours, 5 in 8 hours, 9 in 9 hours, and 3 in 10 hours. Many cases are, however, prolonged for several days or a week, and, occasionally, for several weeks. In a case reported by St. George[9] death was delayed for 3 months.

Treatment.—In most cases of arsenical poisoning the active vomiting removes practically all the food residue in the stomach, but, if the arsenic be taken in the solid form, much of it may adhere to the walls of the stomach, so that the repeated vomiting does not carry it out. If the case should be one in which there is little or no vomiting, the first indication is to produce emesis by the hypodermic administration of apomorphine hydrochloride ($^1/_{10}$ grain) or by the use of such an emetic as warm mustard water. After the stomach is apparently free from food residue copious and frequent gastric lavage should be practiced, the washings being tested with Reinsch's test to determine whether or not arsenic is being removed. One may then administer 4 or 6 ounces of the official arsenic antidote (*Ferri Hydroxidum cum Magnesii Oxido*), which may be extemporaneously prepared by diluting ½ ounce of *tinctura ferri chloridi* with 6 ounces of water and adding magnesium oxide in excess. There is some question as to the value of this antidote, but it is worth a trial and may serve to convert the arsenic remaining in the stomach into a soluble form. If it is used at all, it is wise to repeat it at intervals for a day or so. In any case, copious lavage should follow the antidote, as well as precede it, so that the value may rest entirely with the lavage. Following the gastric treatment, the bowels may be emptied by a saline cathartic, as these act promptly. However, if vomiting and purging have been repeated and copious, it may be wise to attempt to combat the dehydration of the tissues by the administration of large volumes of water and milk, which treatment will, also, have a tendency to increase the elimination of arsenic through the kidney.

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[1] *Medical Jurisprudence and Toxicology*, 4th ed., 1921, p. 676.

[2] Richmond and Louisville Med. Jour., 1873, **15**, 383.

[3] Amer. Jour. Med. Sci., 1858, n. s., **36**, 77.

[4] *On Poisons*, 1875, p. 303; Medical Jurisprudence, 6th Ed., 1910, **2**, 483.

[5] Lancet, 1845, **2**, 432.

[6] Finlay, Lancet, 1883, **2**, 943.

[7] See Foster, Ibid., 1840–41, **2**, 305; Dieberg, Friedr. Bl. f. ger. Med., 1866, **17**, 53; Clegg, cited by Taylor, *On Poisons*, 1875, p. 303.

[8] Toxicology, 1911, p. 454.

[9] Brit. Med. Jour., 1921, **1**, 192.

In the treatment of acute cases, as, also, in the handling of the arsenical dermatitis, the intravenous injection of sodium thiosulphate as well as its oral administration has been advised, the method of administration having been outlined on page 449. The results by this method have been very satisfactory in the hands of some workers, while others have not been so successful in the acute cases. However, there seems little doubt that the sodium thiosulphate treatment is effective in the handling of the dermatitis, especially that following the use of the organic arsenicals.[1] In the acute cases there seems to be some question as to the influence of sodium thiosulphate on the elimination of arsenic, Kuhn and Reese[2] stating that its administration "was followed in each case by an increase in the excretion of arsenic in the urine", while Young[3] shows that in most instances the thiosulphate has markedly diminished the rate of excretion of arsenic and has never increased it, even when there is pronounced diuresis.

The collapse is to be treated with the usual stimulants. In treating the neuritis little is to be expected by attempts to increase the elimination of the arsenic as the damage has already been done. Some value may be forthcoming from frequent, short applications of galvanic therapy and massage. In the chronic cases, the patient should be removed as quickly as possible from the source of the poisoning, and should be handled symptomatically.

Postmortem Appearances.—Arsenic, when applied to any part of the body during life, irritates it markedly, so that phenomena of irritation appear very soon and make rapid progress. It blisters the skin much like a burn would do and corrodes the mucous membranes. Its internal action seems to be directed toward producing fatty degeneration of the parenchymatous organs, especially the liver and the kidneys, while its long-continued action produces considerable degeneration of the nervous tissues.

In the very acute cases there are practically no external signs of the severity of the arsenical action, but in the subacute cases, in which life has lasted for several days, the eyes are much sunken, there is cyanosis of the face, hands, and feet, and jaundice along with skin eruptions or

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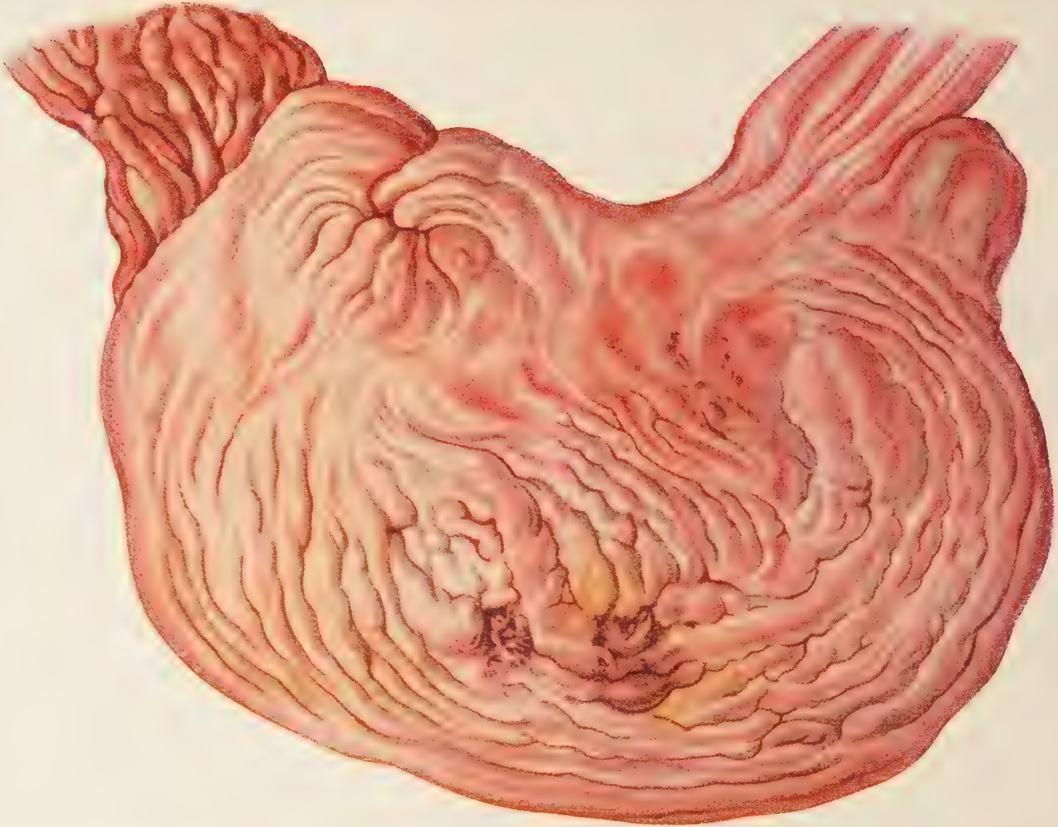
[1] In this connection see Ravaut, Presse méd., 1920, **28**, 73; McBride and Dennie, Arch. Dermat. and Syph., 1923, **7**, 63; Hoffmann and Schreus, Münch. med. Wchnschr., 1923, **70**, 1481; Semon, Brit. Med. Jour., 1924, **1**, 662; Dennie and McBride, Jour. Amer. Med. Assoc., 1924, **83**, 2082; Fuss and Dahlman, Munch. med. Wchnschr., 1925, **72**, 345; Lawson, Jackson and Cattanach, Jour. Amer. Med. Assoc., 1925, **85**, 24; Kuhn and Reese, Ibid., 1804; Haag and Bond, Ibid., 1927, **88**, 1219.

[2] Jour. Amer. Med. Assoc., 1925, **85**, 1804.

[3] Jour. Lab. & Clin. Med., 1928, **13**, 622.

PLATE III



Stomach from a Case of Acute Arsenical Poisoning (Von Hofmann). A woman aged twenty-nine years was poisoned with arsenic. On May 27th she was first taken with vomiting and diarrhea, eventuating in death on June 4th. Though there had been seven days' profuse vomiting and diarrhea, a considerable quantity of arsenic was found in the dead body. She had no systematic medical attention. The necropsy showed a flabby, yellowish, and dilated heart, with cloudy swelling of the muscular fibers. Both the liver and kidneys were the seats of parenchymatous degeneration.

The stomach was moderately distended with a watery, turbid, bloody fluid. The inner wall was markedly swelled, softened, and congested. On the crests of the rugae were ecchymotic points closely set, and mixed with them were injected vessels. At the middle of the greater curvature were dark red, circumscribed areas of confluent ecchymoses denuded of epithelium. Upon and around these areas was a fine, smooth, bright yellow deposit. The intestines contained a large quantity of watery, turbid fluid resembling rice-water. The mucous membrane was pale violet in color and minutely injected. Its epithelium was loose and easily separated.

slight hemorrhages may be noted. While the upper part of the alimentary tract may show no signs of the irritative action, yet, in some cases the throat and esophagus may show reddened patches and erosions of the mucosa from the action of the arsenic brought up in the repeated acts of vomiting.

Usually, more or less marked changes are observed in the *stomach.* The sub-peritoneal vessels of the stomach are generally filled with a thick dark-colored blood. In acute cases especially, the stomach contains a thick, viscid mucus, often tinged with blood or bile. The mucous membrane is swollen and thickened, at times somewhat spongy, and may be grayish-yellow in color or markedly reddened. This redness may extend over the entire surface or, more frequently, may be limited to certain areas, especially on the folds of the rugae. In places, one may find particles of solid arsenic trioxide mixed with the mucus, the mucous membrane showing special signs of swelling and erosion at such points. Tidy[1] believes that the studding of the mucous membrane with minute petechiae, arranged in striations stretching in somewhat curved lines between the cardia and pylorus or found more or less generally over the entire mucous membrane, are especially characteristic of arsenical poisoning. In places where arsenic in substance has lain, one may occasionally see croupous membranes. Occasionally, localized gangrene may ensue, but rarely does the inflammatory process progress to the point of ulceration or perforation. In some acute cases, even when the autopsy is made promptly, and in most cases in which the body has been buried for some time, the mucous membrane may show a bright yellow color, with bright yellow spots on the rugae, due to the action of H_2S upon the trioxide. In the more chronic cases, according to Schwarzacher[2], a generalized yellow color of the gastric mucosa may be observed as a result of fatty degeneration.

It is to be recalled that these gastric changes, and, especially, those found in the small intestine, may be noticed in some degree no matter what the route of administration, although the time of appearance is slower than when the arsenic is ingested by the oral route. Further, it is to be said that, although the above changes are ordinarily found in cases of arsenical poisoning, yet there are undoubted instances reported in which no signs of inflammation may be detected in the stomach. Thus Haines[3] states that, in the case of Lucy Heidelmeyer, "the stomach and bowels showed not the slightest evidence of irritation, but, on the contrary, the mucous membrane was paler than usual."

The changes in the *small intestine* are slight in the very acute cases, but in the subacute forms, where death has not occurred for a day or so, the changes may be quite characteristic. There is usually a diffuse redness, with scattered patches of a deeper hue, and the contents may be bloody, or, occasionally, yellow from the formation of arsenic trisulphide. Multiple ecchymoses throughout the intestinal tract may be seen. The large intestine may be denuded of mucous membrane, but, as a rule, the changes are not so marked as those in the small bowel.

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[1] See Woodman and Tidy, *Forensic Medicine and Toxicology*, 1877, p. 142.

[2] Deutsche Ztschr. f. d. ges. ger. Med., 1927, **9**, 257.

[3] See Peterson, Haines and Webster, 1923, **2**, 38.

In protracted cases fatty degeneration of the liver, kidneys and heart muscle are ordinarily found, being the more marked the longer the illness has lasted. The gross appearance of the kidneys may suggest mercuric poisoning, as pointed out by Marx[1], while Hofmann-Haberda[2] mentions the fact that in one case of acute poisoning calcium infarcts were found in the kidneys. Ecchymoses may be found in the epicardium and, also, in the endocardium, especially of the left ventricle, which are quite characteristic even if death occurs on the first day.[3]

Detection.—Owing to the fact that arsenic is liable to gain entrance into the human body from so many extraneous sources, the finding of a mere trace of this poison in the tissues can not be taken as absolute proof of an actual poisoning, without further evidence either from the history of the symptoms and the postmortem findings, or from the circumstances surrounding the case. A further point to be remembered by the toxicologist is the fact that the soil of many cemeteries may contain quite appreciable traces of arsenic, so that in the examination of exhumed bodies, especially, those in which the coffin may have been destroyed and the body have come in contact with such soil, arsenic may have been taken up by postmortem imbibition. In such cases, it is advisable that a portion of the soil adjacent to the body be taken for analysis, in order that a check may be furnished on such a possibility. Occasionally the toxicologist is called upon to examine the remains of a cremated body. While it is true that some of the arsenic may be lost by volatilization, yet it is possible to detect arsenic in such ashes, especially in the remains of the larger calcined bones, as has been shown by Mai and Hurt[4]. Jesser[5] in some experimental work has shown that marked traces of arsenic were found in the ash of each of 9 bodies, when their cremation was preceded by that of a body into which 1 gram of arsenous acid had been injected. Remund[6] shows that arsenic may be detected in crematory ashes, but only in amounts of 5 to 10 per cent of the total arsenic originally present. In this connection it must be stated that arsenic may be found in such ashes as a contamination from the iron nails and screws of the coffin, so that absolute proof of a poisoning may, even here, be a very difficult matter. Of course, if the body has been embalmed with arsenical fluid before the obtaining of the organs for chemical examination, the detection of even large quantities of arsenic has absolutely no value in forensic cases, except when crystals of solid arsenic trioxide are found in the stomach. It is for this reason that most of our states now prohibit the use of arsenical embalming fluids.

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[1] Deutsche Ztschr. f. d. ges. ger. Med., 1927, **11**, 36.

[2] *Lehrbuch der gerichtlichen Medizin,* 11te. Aufl., 1927, 840.

[3] See Hofmann-Haberda, *Loc. cit.*, p. 840; and Schwarzacher, Deutsche Ztschr. f. d. ges. ger. Med., 1927, **9**, 257.

[4] Ztschr. f. angew. Chem., 1904, **17**, 1601. See, also, Mai, Ztschr. f. anal. Chem., 1904, **43**, 617; and Popp. Ztschr. f. angew. Chem., 1928, **41**, 856.

[5] Deutsches Ztschr. f. d. ges. ger. Med., 1926, **8**, 275.

[6] Deutsch. Ztschr. f. d. ges. ger. Med., 1929, **13**, 33.

In a toxicological examination for the presence of arsenic, it is very important that the analyst be furnished with some other organs than the stomach and intestines, as the stomach, especially in protracted cases, may contain little or no arsenic. The organs of special value are the liver and kidneys, while all of the tissues will yield their quota of arsenic in the ordinary case. As the detection of arsenic in the liver and kidneys is proof of its absorption, the evidence of poisoning is stronger when these organs are examined than if arsenic be found simply in the stomach. It is to be recalled that the arsenic in the stomach has, for the most part, had little to do with the actual death, as the symptoms, even of gastric irritation, are, probably, the result of changes brought about after absorption rather than by the direct action of arsenic on the tissues themselves. Further, the stomach may contain a large amount of arsenic and very little of it may have been absorbed, so that death may, in reality, be due to some cause other than actual arsenical poisoning.

Preliminary Tests.—In the examination of stomach contents, feces, or tissues, it is occasionally advisable to make certain preliminary tests to ascertain whether or not arsenic is present, at least in appreciable amounts. If the careful inspection of the gastric contents reveals white crystalline material, this may be carefully washed with water to remove extraneous matter and submitted to the sublimation test, which will show a crystalline sublimate of arsenic trioxide consisting of octahedral forms, and, occasionally, of tetrahedra or dodecahedra, if the crystals are white arsenic. If the material under examination is thought to be Paris green, orpiment, realgar, potassium arsenite, etc., it may be dried and mixed with a well-dried mixture of 3 parts of anhydrous sodium carbonate and 1 part of potassium cyanide. On heating this mixture in a reduction tube, metallic arsenic is deposited in the cooler portions of the tube as a mirror-like ring of a black, shading to brown or gray, color.

Reinsch's Test.—While there are a large number of tests for both the trivalent and pentavalent forms of inorganic arsenic, yet most of these can not be applied until the arsenic is brought into solution and the organic matter completely destroyed. The test of Reinsch[1] is of special value in forensic cases as it permits an examination of tissues, stomach contents, urine and feces without any previous destruction of the organic matter and, when properly applied, yields results which are extremely delicate, speedily obtained, and highly reliable. The method of performing this test has been outlined on page 466. As both the copper foil and the hydrochloric acid used in the test may contain arsenic as an impurity, it is essential that blank tests be made with these reagents before they are employed in the test itself. If arsenic be present in the tissues examined, in the form of arsenites, the deposit on the copper may appear as a steel-gray, purple or even black deposit, while if the amount of arsenic be very large the deposit may be easily scratched off in the form of flakes. If the arsenic be present in the form of arsenates, a deposit will not form readily and then only if the solution be some what concentrated. If pentavalent arsenic is suspected, it is wise to treat the material under investigation with a little sodium sulphite to reduce the arsenic to the arsenous (trivalent) form, heating the acid mixture afterwards until the excess sulphurous acid is removed, or one may add a few crystals of ferrous sulphate, as suggested by Blunt[1], when the coating on the copper will appear in a short time.

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[1] Jour. f. prakt. Chem., 1841, **24,** 244. *Das Arsenik,* Nürnberg, 1843.

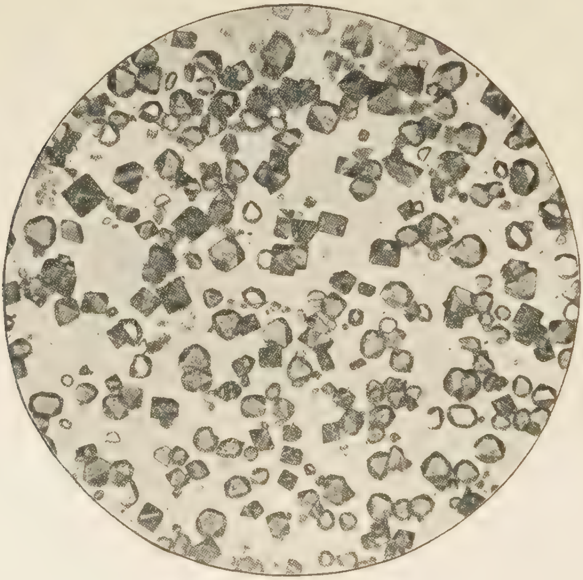

Fig. 41.—Sublimate of arsenic trioxid (magnified 340 diameters). (Holland in, Peterson, Haines and Webster, "Legal Medicine and Toxicology.")

As stated on page 467, there are several substances other than arsenic that give a coating on the copper foil under the conditions of this test, especially important among these being mercury and antimony. For this reason one is never justified in making an absolute statement that arsenic is present without going a step further. To verify the arsenical film, the copper slip is washed in water, alcohol and ether, dried between filter paper, and either rolled into a small cylinder or preferably cut into pieces with scissors, as by this latter process there is less danger of getting fat particles on the copper. The stained pieces of copper are now placed in a small glass tube, about 10 cm. long and 5 mm. wide, and heat applied to the lower end, the tube being held at an angle of about 45 degrees. If arsenic be present, it will sublime and be deposited on the cooler portions of the tube in the form of octahedral crystals, or some modification of this type. As previously stated, mercury volatilizes, under these conditions, in the form of globules, while antimony sublimes and is deposited in an amorphous form. The crystals of the arsenical deposit should be in well-defined form, the larger ones being nearer the point of application of heat, while the smaller ones are higher up in the tube.

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[1] Analyst, 1923, 48, 596.

While the deposit on the copper is really an alloy of copper and arsenic, the sublimate is arsenic trioxide and may be proven to be an arsenical compound by dissolving in boiling water and applying such tests as the ammoniosulphate of copper test, the ammonionitrate of silver test, the Bettendorff test, or may be precipitated by H_2S and the resulting arsenous sulphide submitted to the reduction test with the formation of the metallic arsenical mirror.

While this test is extremely delicate and yields prompt results with trivalent arsenic, it may be made to respond promptly to pentavalent arsenic by heating with sodium sulphite or by adding ferrous sulphate as previously stated. However, the presence of such oxidizing agents as nitric acid, potassium chlorate, and manganese dioxide prevent the formation of a coating as they have a tendency to dissolve the copper. If such substances are suspected, evaporate the material to dryness with excess of hydrochloric acid in order to expel the nitric acid and free chlorine, take up the residue with water, acidify with hydrochloric acid and apply the test. Many of the organic arsenicals do not respond to this test.

If applied in the manner described and if all interfering substances are removed, this test will detect 0.0001 grain (0.0065 mg.) of arsenic, while, when special tubes were employed, Wormley[1] was able to detect 0.00002 grain (0.0013 mg.). The delicacy of this test is such that negative results almost preclude the possibility of arsenic being a factor in a case of forensic interest, as the quantities of tissue employed in the test will, almost certainly, contain more than 0.0001 grain of arsenic if the case be one of arsenical poisoning. The test has a special advantage in that it permits a rapid and certain method of detecting arsenic, mercury or antimony in stomach contents prior to death and may, therefore, lead to prompt treatment, which might otherwise be neglected.

Gosio's Test.—This test is a purely qualitative one, but it is extremely delicate and may, like the Reinsch test, be employed upon material which has not been decomposed. It is based on the fact that the growth of molds in the presence of arsenical compounds evolves a gaseous substance, probably diethylarsine, which has a garlic-like odor, which is very lasting and penetrating. While Gosio[2] found *Penicillium brevicaule* was especially effective in the production of this gaseous compound, Schmidt[3] found 13 species of molds acting similarly.

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[1] *Micro-Chemistry of Poisons*, 2nd Ed., 1885, p. 274.

[2] Arch. ital. de Biol., 1892, **18**, 253.

[3] Dissertation, Erlangen, 1900.

Prepare a culture of the mold upon potato slants in the usual manner, incubating the transplant for 1 to 2 weeks. Mix in a test-tube about 5 grams of the finely hashed tissue with 10 grams of rasped raw potato, or as advised by Abel and Buttenberg[1] with rye bread crumbs, stopper with cotton and sterilize in the autoclave. Allow this tube to cool and inoculate the material with the spores of the mold, allowing the tube to stand in the incubator for 12 to 72 hours. At the end of this period the peculiar, penetrating garlic-like odor of diethylarsine will be observed if arsenic be present.

Tellurium and selenium also evolve a somewhat similar gaseous compound under the conditions of this test, but such substances are not likely to be involved in a toxicological case. Antimony does not yield a gas with this test, so that this metal is ruled out by this test, whereas it may be shown in the Reinsch test. The delicacy of this test is such that 0.00001 gram of As_2O_3 is readily detected.

Determination.—Having proven that arsenic is present in the tissues under investigation, a quantitative determination may be made in several ways, the method of choice being determined somewhat by the relative amount of arsenic shown to be present by the Reinsch test. In all the quantitative methods it is essential that the organic matter be destroyed before application of the special test decided upon.

Method of Fresenius and Von Babo.—This method[2] has the advantage over the other quantitative tests to be described that it permits the detection and determination of all metallic poisons without further treatment of the tissues, while the other tests are limited to the estimation of arsenic only. The method of destruction of the organic matter has already been described on page 340. In the systematic examination for inorganic poisons by this method, arsenic, if present, will be found along with all other metals of the 5th and 6th groups in the precipitate produced by H_2S in the filtrate from the destruction of the organic matter. After obtaining the precipitate of sulphides, as previously discussed, these are filtered off and washed with hydrogen sulphide water until the washings no longer show a reaction for the chlorine ion. This precipitate is then purified, to remove the traces of organic matter which may have been precipitated with the metallic sulphides, as follows: Place the filter with the sulphides in a small evaporating dish and heat on the water bath until thoroughly dry. Moisten the residue with concentrated nitric acid (free from chlorine) added drop by drop and evaporate to dryness on the water bath, repeating the process if necessary. Now moisten the residue uniformly with concentrated sulphuric acid and heat on the water bath for 1 or 2 hours, finally at a somewhat higher temperature in an air, sand or oil bath, until the carbonized mass becomes friable, the temperature being raised until sulphuric acid vapors begin to escape. Now remove the dish from the hot bath, allow to cool, and heat the friable, carbonaceous residue on the water bath with a mixture of dilute hydrochloric acid (1:8), the mixture being stirred and the residue pressed with a glass rod in order to facilitate the solution of the arsenic. Filter the solution and repeat the extraction with more dilute acid, washing the residue on the filter with hot dilute acid. This colorless or at most very slightly yellowish solution is then treated with a little sodium sulphite to reduce the arsenic to the arsenous form and the mixture heated until the excess of sulphur dioxide is expelled. Filter the solution, if necessary to remove any residue of sulphur, and saturate the solution with H_2S, first with gentle heating and then without heat as previously discussed on page 341.

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[1] Ztschr. f. Hyg., 1899, **32**, 449.

[2] See Fresenius, *Qualitative Chemical Analysis*, 17th Amer. Ed., 1921, p. 739.

If there is reason to believe that no other metals than arsenic are present, the pure yellow precipitate of arsenous sulphide is filtered on a dried and weighed filter, is washed with water, then with alcohol followed by either benzene or petroleum ether to remove any sulphur present, and finally again with alcohol to remove the sulphur solvent. Dry the filter and precipitate at 100° to constant weight. One part of arsenous sulphide corresponds to 0.8042 part of arsenic trioxide or to 0.6092 part of metallic arsenic.

Should the preliminary tests have indicated the possible presence of other metals along with arsenic, the precipitate of the sulphides at this point must be subjected to further treatment to separate out the arsenic and, also, to obtain the other metals in such a state that they may be determined. In such a contingency procede as follows: Filter off the precipitate of sulphides and wash thoroughly with hydrogen sulphide water. Pierce the point of the filter and wash the precipitate from the filter with a jet of water, using as little water as possible. Treat the liquid in which the precipitate is suspended with ammonium hydroxide and then with ammonium sulphide solution and digest at a gentle heat for a few minutes. In this process the sulphides of arsenic, antimony and tin will completely dissolve, while a small amount of the sulphide of copper, if present, will also pass into solution. Now filter, wash the residue with hot water and evaporate the filtrate and washings to dryness in a porcelain dish. Treat this residue with a little concentrated nitric acid and again evaporate to dryness. Intimately mix this residue with about 3 times its amount of a mixture of 1 part of dry sodium carbonate and 2 parts of sodium nitrate and thoroughly dry this mixture over the water bath. Introduce portions of this dry material, a little at a time, into a porcelain crucible, which contains some sodium nitrate heated to redness and, as soon as all of the residue is added, heat the crucible very gradually until the fused mass becomes colorless[1]. Allow the fused mass to cool and extract it with warm water, washing the material into a small flask. Add a little sodium bicarbonate in order to precipitate whatever tin may have been in solution as stannic oxide, filter and wash the residue on the filter with a mixture of equal parts of alcohol and water. The filtrate will contain the arsenic as sodium arsenate, while the insoluble residue contains, if they be present, antimony as sodium pyroantimonate, tin in the form of the oxide, and copper as the oxide.

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[1] If copper sulphide has been dissolved by the ammonium sulphide in the extraction of the arsenic from the mixed sulphides, the fused mass will remain gray or even black.

Concentrate the filtrate and washings to remove the alcohol, carefully acidify the mixture with pure dilute sulphuric acid and heat in a porcelain dish almost to dryness. Now add a little concentrated sulphuric acid and heat until dense white fumes of sulphuric acid are given off, in order to insure the expulsion of nitric and nitrous acids. Allow the solution to cool, dilute with water, add a little sodium sulphite to reduce the pentavalent arsenic to the trivalent form, and heat until the excess of sulphur dioxide is given off. The arsenic is then precipitated as arsenous sulphide as above described and weighed as such.

Marsh Test.—This test[1] is possibly the most delicate and reliable of the tests for arsenic, provided all the details are carefully checked and all interfering substances avoided. The test is based upon the facts that (1) when nascent hydrogen is generated in the presence of compounds of arsenic, either of the arsenic or arsenous types, arseniuretted hydrogen (arsine, AsH_3) is developed, and (2) when this gas passes through glass tubes heated to redness, the arsine is decomposed into metallic arsenic and hydrogen, the former being deposited, in the form of a mirror, in the cooler portions of the tube. As arseniuretted hydrogen is very poisonous, extreme care must be exercised when working with this test. The Marsh test may be employed both for qualitative detection and quantitative determination of arsenic, being of special value when small quantities are in question.

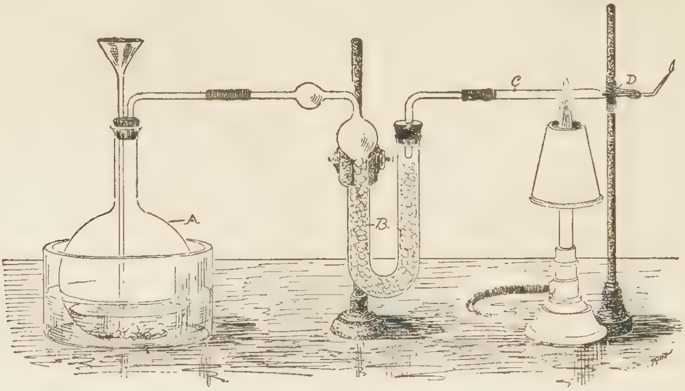

FIG. 42.—Marsh apparatus for the detection of arsenic and antimony. A, Hydrogen generator; B, calcium chloride drying-tube; C, hard glass tube; D, arsenic mirror. (From Autenrieth and Warren "Detection of Poisons" P. Blakiston's Son & Co. Publishers.)

For *qualitative* purposes the test is performed as follows: In a flask arranged for generating hydrogen (Fig. 42), with air-tight connections

[1] London Med. Gaz., 1836, 18, 650.

(corks and not rubber stoppers being used), place 15 to 25 grams of pure arsenic-free zinc and pour through the thistle-tube (b) cold dilute (1:6) sulphuric acid. The evolution of the hydrogen should not be allowed to get too rapid, as the liquid in the flask may get too warm and, as a result, some of the sulphuric acid may be reduced to sulphurous acid or, possible, to hydrogen sulphide, which may interfere with or actually prevent the detection of arsenic. Should the flask become very hot, set it in a dish of cold water. The gas is conducted first through a drying-tube containing calcium chloride between plugs of glass wool, and then through an exit-tube of hard glass, about 5 mm. internal diameter and 25 to 50 cm. long, which is turned up at the end and drawn out at the tip to make a jet. After waiting a few minutes (ordinarily 5 to 10) for the air in the apparatus to be expelled[1], a Bunsen flame is applied in the course of the exit-tube, which should be heated red-hot. If no stain appears on the glass beyond the point of heating after 15 minutes, the chemicals may be regarded as free from arsenic. Having proven that the reagents used in the test are free from arsenic and having ignited the gas at the jet, introduce through the thistle-tube the suspected arsenical solution, which should not contain organic matter, free nitric acid and, preferably, any hydrochloric acid. Probably the best material to employ is the sulphuric acid solution of the fusion described on page 511, which answers all the requirements of this test. The solution is introduced in small portions, care being taken that the evolution of the hydrogen is not too rapid at this juncture. At the same time heat the ignition tube to redness a little ways back of the bend[2]. If the fluid added contains arsenic, all of the arsenic passing through the heated tube will condense as a mirror-like ring of a black shading to brown or gray color. The extent of this mirror-like deposit gives some evidence as to the amount of arsenic present, and, with certain modifications to be spoken of below, may give very exact quantitative results. If the flame be now removed from the ignition tube, the flame at the jet will now burn with a bluish-white flame, arsenic trioxide and water being formed. If a cold porcelain surface be depressed upon this flame only the hydrogen burns, while the arsenic is deposited on the porcelain as the so-called arsenic spot, which is black or brownish in color. If the solution to be tested contained arsenic in the *arsenic* form the reaction is slower in appearing than when the substance is in the arsenous form.

It is to be said that antimony is deposited under the same conditions as is arsenic, although the antimony ring is closer to the flame than is the arsenic and is more tin-like in luster than the arsenic mirror. However, these points do not serve for forensic differentiation. The following tests will serve to show whether the spots on porcelain are due to arsenic or to antimony: (1) The arsenic stains are soluble in warm solution of chlorinated lime or soda, while the antimony spots are insoluble or very sparingly soluble; (2) If the spot be dissolved by heating with a few drops of a solution of ammonium molybdate in nitric acid, a yellow precipitate of ammonium arsenomolybdate is formed if the spot be arsenical, while if antimonial no precipitate is formed; (3) if the spot be dissolved in nitric acid and dried by careful heating a whitish residue is left, which turns red when touched with a drop of silver nitrate solution, if the stain be arsenical, while if antimonial no change of color is noticed; (4) another spot, if arsenical, dissolves in ammonium sulphide and on evaporation leaves a yellow stain soluble in ammonia, but insoluble in hydrochloric acid; while, if the residue is antimonial, the sulphide is orange-red, and is insoluble in ammonia, but soluble in strong hydrochloric acid. Arbuckle and Thies[1] have called attention to the finding that, if hydrochloric acid be used in the Marsh apparatus, a metallic mirror similar to those given by arsenic and antimony, will be formed by the zinc, but that no such spot forms in the presence of sulphuric acid, this spot being differentiated from the usual spots by the fact that it dissolves readily in dilute acids.

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[1] To tell when this point is reached, collect some of the evolved hydrogen in an inverted dry test-tube and apply a flame. If the hydrogen ignites without any detonation, the air is assumed to be out of the apparatus. As a precaution, it is always wise to cover the flask with a towel before igniting the gas at the exit-tube, as dangerous explosions sometimes do occur.

[2] The best results are obtained if the tube be constricted to a small caliber at one or two points just beyond the part heated, as the mirror will form in the constricted portion and be somewhat more visible.

The proper development of the arsenical mirror or the formation of the arsenic spots is interfered with by the presence of hydrochloric acid, free chlorine, nitric[2] or nitrous acids, and salts of silver and mercury (especially mercuric chloride), as they may decompose the arsine in the flask as soon as it is generated and, thus, prevent its reaching the ignition tube. However, if the solution has been properly prepared before introduction into the generating flask, none of these interfering substances will be present.

A further method of detecting arsenic by the use of the Marsh apparatus consists in extinguishing the flame at the exit-tube and allowing the generated gas to pass into a solution of dilute neutral silver nitrate. The arsine darkens this solution, precipitating black metallic silver and leaving in the solution arsenous acid and free nitric acid. This solution may be filtered, neutralized with alkali and tested by the various qualitative tests for arsenic mentioned on page 507.

For *quantitative* determination of relatively small amounts of arsenic, the mirror is allowed to develop during several hours and the tube is cut off at a safe distance from the deposit in the constricted portion of the tube, and the tube with its mirror weighed at once. The arsenic is then dissolved out with nitric acid, the tube rinsed well with water, dried with alcohol and ether and again weighed. The loss in weight represents the weight of elementary arsenic deposited from the amount of material added to the generating flask. This quantitative determination is more applicable to the smaller amounts of arsenic than to the larger ones, as so much arsine may be developed, in the presence of large quantities of arsenic, that it may not all be condensed on the tube and, further, the period of evolution of arsine may not be made long enough to permit the obtaining of the full amount in the mirror. Where such small amounts as 0.02 mg. or less are to be determined, it is preferable to compare the mirror formed from the unknown solution with standard mirrors prepared from known amounts of arsenic and preserved in an atmosphere of hydrogen. The probable limit of delicacy of the Marsh test, where the arsine is allowed to pass through constricted tubes heated to red heat and cooled beyond the point of application of heat, is 0.001 mg. (0.000015 grain), although with special modifications it may be made to reach 0.0001 mg. Instead of using the chemical means of generating hydrogen, electrolysis of dilute sulphuric acid by the galvanic current may be employed and has some advantages, as the current of hydrogen is regulated to better advantage and is kept more or less constant during the process.

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[1] Jour. Elisha Mitchell Sci. Soc., 1927, **43**, 50. Abstract in Chem. Abst., 1928, **22**, 1117.

[2] See Schoofs, Bull. soc. chim. Belg., 1926, **35**, 121. Abstract, Chem. Abs., 1926, **20**, 3663.

Gutzeit Test.—This test[1] is based on the fact that arsine develops a yellow color by its action on a concentrated solution of silver nitrate and this compound is immediately decomposed by water with the formation of black, finely divided silver. The application of the qualitative test is, however, different from that mentioned above under the Marsh test.

In a test-tube place 1 cc. of the suspected sulphuric acid solution as in the Marsh test (urine or stomach contents may be used), add about 1 gram of chemically pure zinc and 5 cc. of dilute sulphuric acid (6 per cent.), and insert in the upper part of the tube a plug of absorbent cotton moistened with lead acetate (to catch any hydrogen sulphide that may be developed). Now clasp over the top of the tube a cap made of three layers of filter-paper, moistening the upper layer with a drop or two of a saturated solution of silver nitrate, and set the tube aside in a dark place for a time. If arsenic be present a lemon-yellow stain is produced on the top layer of paper, which gradually turns brown and then black from the border inward, if the exposure be continued, or turns black immediately when moistened with water. Under the same conditions antimony will produce a spot on the filter paper, but this spot is not yellow, but brown, and is not blackened at once by water. Phosphine, if present, will give a yellow stain, which becomes black with water. This test will detect 0.01 mg. of arsenic, but it is not as characteristic as some of the other tests for arsenic.[2]

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[1] Pharm. Ztg., 1879, p. 263.

[2] If the arsine be developed by the action of sodium or potassium hydroxide on zinc or aluminum, as in *Fleitmann's* test, arsenic reacts with the production of the black stain on the filter paper moistened with silver nitrate solution, while no reaction is observed with antimony. However, phosphine will react in the same way as with the Gutzeit test.

Modified Gutzeit Test.—Modifications of the Gutzeit test have been recommended for *quantitative determination* of the arsenic and have been found so simple, so reliable, and so delicate, that they are probably more widely used at the present time than other methods for the estimation of the amount of arsenic present in food products, commercial articles, and in human tissues.

Flückiger[1] recommended that mercuric chloride be employed for the detection of arsine instead of silver nitrate, as the yellow spot produced by the action of the arsine is not affected by either light or water, as is the silver spot. Goode and Perkin[2] showed that the coloration produced with mercuric bromide was more stable than that given by the chloride, while Smith[3] showed that the bromide is more sensitive than the chloride of mercury toward arsine and recommended a modification of the method of Sanger and Black[4], which is now widely employed. While the usual method of performing this quantitative test employs the chemical means of generating hydrogen, several modifications have been advocated in which electrolytic methods are used[5], which yield very satisfactory, reliable and extremely delicate results, but we shall describe only the usual chemical method.[6] While this method was devised for determination of small amounts of arsenic in food and drug products, it is easily applicable to urine, feces, stomach contents and tissues, where the amounts of arsenic are small. If the arsenic is large in amount, the determination would better be made by the direct method of weighing the sulphide as previously discussed, because such large amounts do not lend themselves easily to this test unless very small amounts of tissue are used and, under these circumstances, the distribution may be regarded as not absolutely uniform throughout the remainder of the tissue.

Apparatus.—The apparatus to be used in this test is shown in Fig. 43. The hydrogen generator is a 2 ounce wide-mouthed bottle. This is connected by means of a perforated rubber stopper with a glass tube, 1 cm. in diameter and 6 cm. long, containing a piece of lead acetate paper[7] rolled into a coil. This tube is connected by means of a perforated rubber stopper with a similar tube filled with lead acetate cotton[1], squeezed to remove excess of the solution. The cotton in the tubes employed for all the tests should be uniformly moist to obtain comparative stains. The second tube is connected by means of a perforated rubber stopper with a narrow glass tube, 3 mm. in internal diameter and 12 cm. in length, containing a strip of the mercuric bromide paper[2].

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[1] Arch. d. Pharm., 1889, **222,** 1. See, also, Gotthelf, Jour. Soc. Chem. Ind., 1902, **22,** 191.

[2] Jour. Soc. Chem. Ind., 1906, **25,** 507.

[3] U. S. Dep't. Agr. Bureau of Chemistry Circular 102. See, also, Kemmerer and Schrenk, Jour. Ind. and Eng. Chem., 1926, **18,** 707.

[4] Jour. Soc. Chem. Ind., 1907, **26,** 1115; See, also, Beck and Merres, Arb. a. d. Kais. Ges.-Amt. 1915, **50,** 38.

[5] See Mai and Hurt, Ztschr. f. Unt. d. Nahr.-u. Genussmit., 1905, **9,** 193; Lawson and Scott, Jour. Biol. Chem., 1925, **64,** 23; Osterberg, Ibid., 1928, **76,** 19.

[6] The method here outlined is the official one in Official and Tentative Methods of Analysis of the Association of Official Agricultural Chemists, 2nd ed., 1925, p. 171 and is practically the same as recognized by the U. S. Pharmacopoeia, 10th Revision, 1925, p. 428. See, in this connection, Hann, Jour. Assoc. Off. Agr. Chem., 1922, **6,** 31; Ibid., 1923, **7,** 48.

[7] Soak heavy filter paper in 20 per cent. lead acetate solution, dry, and cut into pieces 4.5 cm. by 16 cm.

Preparation of Solution.—Weigh out 10 to 50 grams of the finely hashed tissue (the amount depending upon the relative quantity of arsenic found by the Reinsch test) and decompose it by the method of Gautier with sulphuric and nitric acids, as discussed on page 342. When the oxidation is complete, remove completely all the nitric and nitrous acids by evaporating to approximately 5 cc., cool, dilute with 10–15 cc. of water and again evaporate until white fumes are evolved. Cool, dilute with water, cool again, and dilute with water to a definite volume (usually 25, 50 or 100 cc. depending upon the richness in arsenic). This solution is then ready for use in the test. Instead of using this method of destruction of the organic matter, one may follow the same procedure as outlined under the Marsh test, employing the sulphuric acid solution of the fusion as there described.

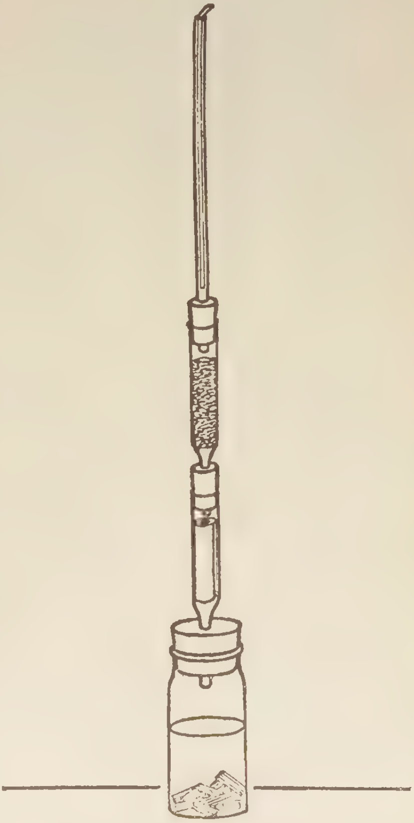

FIG. 43.—Apparatus for the determination of arsenic. (From "Official and Tentative Methods of Analysis of the Association of Official Agricultural Chemists," (2nd. ed.,) 1925.)

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[1] Soak absorbent cotton in 5 per cent. lead acetate solution. In the method of the U. S. Pharmacopoeia, one tube takes the place of these two tubes, and glass wool is used instead of the cotton.

[2] Cut stiff heavy quantitative filter paper (such as Schleicher and Schull's No. 589 or Munktell's Swedish No. 0) into strips exactly 2.5 mm. wide and approximately 12 cm. long. Soak for 5 min. in a 5 per cent. solution of mercuric bromide in 95 per cent. alcohol. Remove the excess of solution by pressing the strips between filter paper and then dry them quickly on glass in an oven heated to 100° C. Place at once in a glass-stoppered wide-mouthed brown bottle and protect from the light.

A very satisfactory method of preparing the solution for use in this test is that given by Lawson and Scott[1] and modified by Osterberg[2]. Ten grams of the tissue are finely hashed and placed in a 500 cc. Pyrex Kjeldahl flask, or 10 cc. of urine, 10 grams of stomach contents, or 10 grams of feces may be used if such material is to be investigated. Add 20 cc. of arsenic-free sulphuric acid, about 5 grams of potassium sulphate, and a crystal of copper sulphate. Heat the flask and contents cautiously at first until the material no longer foams, then more strongly until the solution is colorless, adding more sulphuric acid if this seems necessary. Cool the solution and dilute to 100 cc. in a volumetric flask.

Determination.—Introduce 20 cc. of the solution (prepared as above), or, if the quantity of arsenic be large, an aliquot containing approximately 0.03 mg. of As_2O_3, into the generator and add 20 cc. of dilute sulphuric acid (1:4). If the total volume added to the generator be less than 40 cc., dilute to that volume with water and then add 4 cc. of 20 per cent. potassium iodide solution. Heat to about 90° C., add 3 drops of stannous chloride solution[3], and heat for 10 minutes. Cool the generator and its contents, first in air and then in a pan containing water and ice, to a temperature of about 5° C.; add approximately 15 grams of arsenic free stick zinc, and connect the entire apparatus as mentioned above and as shown in the cut. Keep the generator in ice water for 15 minutes, remove from the bath, and allow the evolution of gas to proceed for an hour longer. Remove the sensitized paper and compare the stain with similar stains produced under like conditions with known quantities of arsenic.[4] The stains, as received on the mercuric bromide paper, will darken slightly if immersed in hydrochloric acid (1:1) for 2 minutes at not over 60° C., while a few minutes treatment with ammonium hydroxide gives them a black color as shown in Plate IV.

Antimony, if present in the material tested, will produce a gray stain in this test. Compounds of sulphur, such as sulphites, sulphides, thiosulphates, and other compounds which liberate hydrogen sulphide or sulphurous acid when treated with sulphuric acid and which would interfere with the test if present, should have been removed by oxidation

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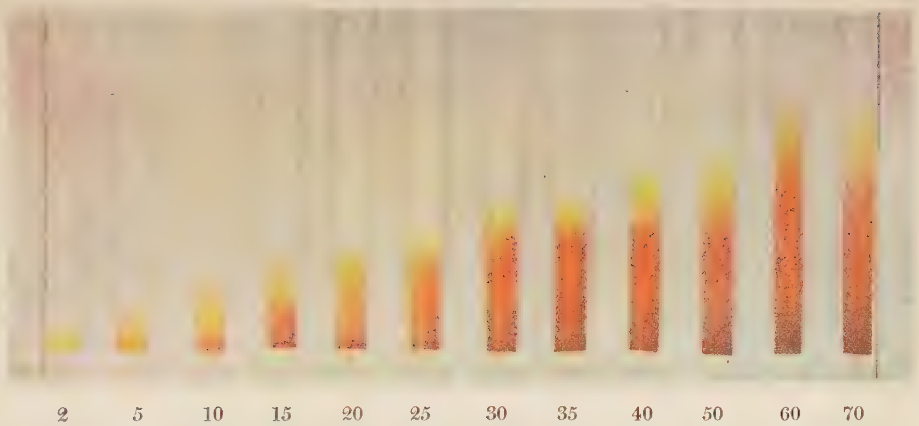
[1] Jour. Biol. Chem., 1925, **64**, 23.

[2] Ibid., 1928, **76**, 19.

[3] Dissolve 40 grams of arsenic-free stannous chloride crystals in sufficient concentrated arsenic-free hydrochloric acid to make 100 cc.

[4] The standard arsenic solution is prepared as follows: Dissolve 0.1 gram of pure arsenic trioxide, which has been finely pulverized, dried over sulphuric acid, and accurately weighed, in about 5 cc. of a 20 per cent. solution of sodium hydroxide (free from arsenic). Neutralize the solution with dilute sulphuric acid (free from arsenic), add 10 cc. of the same acid (1:4) and sufficient recently boiled distilled water to bring the volume to exactly 1000 cc. at 25° C. Accurately measure 10 cc. of this solution, transfer it to a liter flask, add 10 cc. of dilute sulphuric acid and make up the volume with recently boiled water to exactly 1000 cc. This solution contains 0.001 mg. of As_2O_3 per cc. and is the one used in making the standard stains, which are prepared in exactly the same manner as mentioned above for obtaining the stain from the unknown solution. When the standards are prepared, they may be preserved in glass bottles and, if kept in the dark, will last for some time.

PLATE IV


2
5
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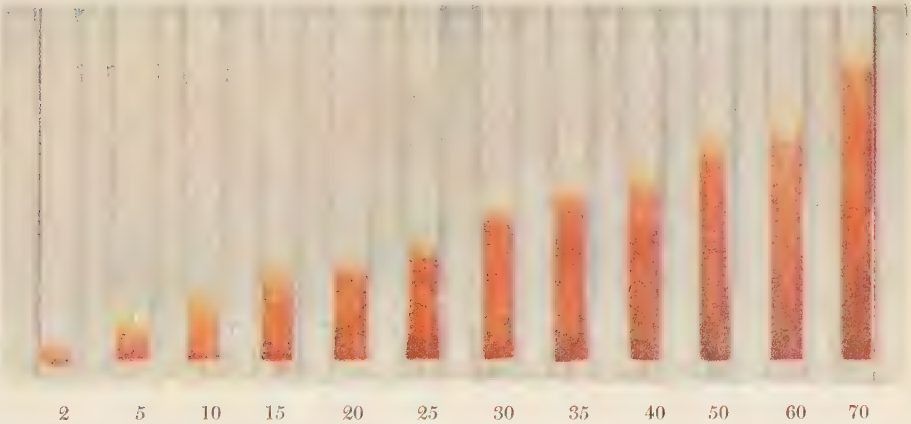
60
70

Standard Arsenic Bands in Micromilligrams of As_2O_3 (Initial).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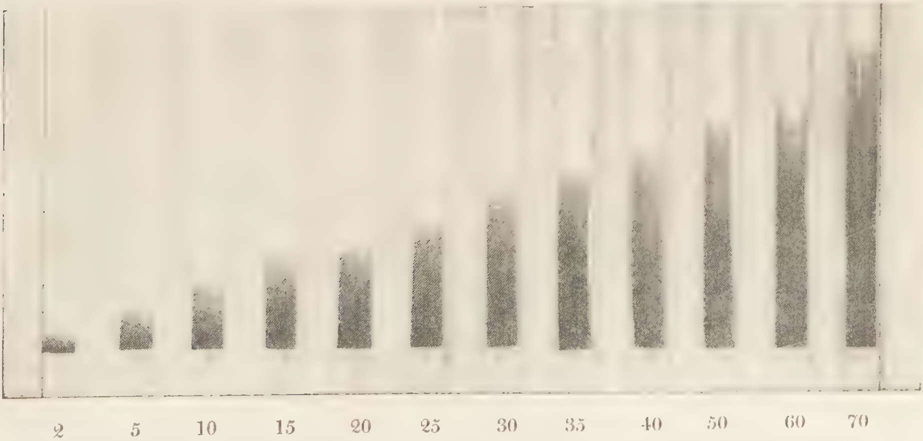
Standard Arsenic Bands in Micromilligrams of As_2O_3 (Hydrochloric Acid Development).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Standard Arsenic Bands in Micromilligrams of As_2O_3 (Ammonia Development).

[From Autenrieth and Warren, "Detection of Poisons," P. Blakiston's Son & Co., Publishers.]

with nitric acid and should not be present in the material to be tested. If by any chance the lead acetate paper should show any blackening during the process, this is evidence that such sulphur compounds have not been completely oxidized and the test must be started over, oxidizing a fresh portion of material. Phosphine, if present, will give a yellow stain, just as in the qualitative Gutzeit test, but this stain may be differentiated from that given by arsenic by moistening it with ammonia, when the arsenic stain will become black, while the one produced by phosphine will not show any change in color.

This test is extremely delicate, the absolute delicacy being set, according to Autenrieth[1] at 0.00008 mg. of arsenic trioxide, but the practical limit is 0.001 mg., although by using a narrower band in a smaller exit-tube the limit may go as low as 0.0005 mg.

ORGANIC ARSENICALS

The organic arsenicals comprise a large group of both aliphatic and aromatic derivatives. As Raiziss and Gavron[2] state, "Although the number of known arsenicals now extends into the thousands, they are all synthetic products with the possible exception of diethylarsine." These organic compounds are, as a rule, much less toxic than are the mineral arsenicals, although it must be stated that the former all possess potential fatal properties under proper conditions. Many of these compounds have been, at one time or another, used in the treatment of trypanosomal and spirochetal diseases, but as more complete knowledge of their toxicity or inefficiency became available, few of them have been retained. In proper doses and under proper conditions the arsenic in these compounds is held in organic combination, being liberated only slowly in the system, but in some cases, without any warning, the arsenic may be split off rapidly and dangerous and even fatal poisoning occur. A typical arsenic reaction probably results only from the compounds containing trivalent arsenic, the pentavalent arsenicals and the arsenobenzene derivatives showing such action only after their arsenic has been converted into this form by means of reduction or partial oxidation respectively. Voegtlin, Dyer and Leonard[3] believe that the toxicity of arsenicals is intimately associated with the sulphydryl constituents of the cell, especially with glutathione. The sulphydryl groups form stable condensation products with arsenic, so that this is held in the organism for considerable periods of time. This conception has been elaborated by the work of Underhill and Dimick[4] and of Walker.[5] It appears doubtful, therefore, that the pentavalent compounds exercise spirocheticidal powers in doses which may not be toxic to the patient[1]. Thus, it has been shown by Nichols[2] that sodium cacodylate has little or no control over the infection with the treponema pallidum, while arrhenal and mon-arsone have no action upon the pathogenic trypanosomes and spirochetes[3], and atoxyl and arsacetin, although possessing quite marked potency against the organisms of sleeping sickness and syphilis, yet were found to have such dangerous effects on the visual organs that their use has been much restricted[4].

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[1] Detection of Poisons, 6th Amer. Ed., 1928, p. 501.

[2] *Organic Arsenical Compounds*, 1923.

[3] Reprint No. 860, Pub. Health Rep., August 17, 1923. See, also, Voegtlin, Physiol. Rev., 1925, **5**, 63.

[4] Jour. Pharm. and Exp. Therap., 1928, **32**, 359.

[5] Biochem. Jour., 1928, **22**, 292.

Trivalent Organic Arsenicals.—While the number of such compounds is great, the only ones which concern us here are the arsphenamines. These compounds apparently have a special affinity for the spirochetes, while their toxicity for the host is comparatively low under ordinary conditions, although it must be remembered that they are all potentially dangerous and may, without any warning, produce fatal poisoning.

Arsphenamine.—This arsenical, introduced in 1910 by Ehrlich and Bertheim under the name of salvarsan ("606"), is now official and is marketed only in sealed ampules of colorless glass, from which the air has been excluded either by the production of a vacuum or by displacement with a non-oxidizing gas. Chemically, arsphenamine is the dihydrochloride of 3-3′ diamino 4-4′ dihydroxy-arseno-benzene ($HCl.NH_2.OH.C_6H_3As{:}AsC_6H_3.OH.NH_2HCl.2H_2O$). Its manufacture and control are regulated by the United States Public Health Service. It is a light yellow powder, odorless or possessing only a very slight odor, and is hygroscopic. It is soluble in water, alcohol and glycerin, but only very slightly soluble in chloroform and in ether. It contains not less than 30 per cent. of arsenic. Tests for its identity may be found in the U. S. Pharmacopoeia.

Though this drug is occasionally given by intramuscular injection, it seems preferable to administer it by the intravenous route in doses ranging from 0.2 to 0.4 gram (3 to 6 grains), although 0.6 gram (9 grains) may be given to an individual, who has been shown to be quite tolerant of the smaller doses. The solution of the drug in water is acid in reaction, but this should not be given without previous neutralization, as the acid solutions are at least 2 to 4 times as toxic as properly alkalinized solutions, the toxicity increasing directly with the concentration[5]. The technic of preparation of the solution for injection is simple but must be carried out carefully, as improper neutralization and manipulation of the solution may lead to increase in toxicity[6]. After opening an ampule the contents should be used at once to prevent oxidation and any unused portion should be discarded. Carelessness in preparing this solution or in handling the solution after preparation have been the cause of severe reactions following the injection. "Emphasis should be laid on the complete physical examination preliminary to administering arsenical treatment, for evidence of renal, cardiovascular, or visceral changes, in the presence of which it should be used cautiously. Weekly urinalyses should be made during treatment. The patient should be questioned concerning any reactions following the last treatment, with special reference to any toxic skin eruptions as danger signals against further treatment. Any evidence of an exfoliative dermatitis is an *absolute contraindication* against any further treatment with any arsenical. Evidence of jaundice should also be looked for and, if present, is an indication for caution." Before starting the treatment, the patient should be given a mild cathartic the night before and should eat no food within 2 or 3 hours before the injection. Only a light meal should be taken a few hours following the injection. Ambulatory patients should rest for a short time after the injection.

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[1] See Voegtlin and Smith, Jour. Pharm and Exp. Therap., 1921, **16**, 449: Schamberg, Raiziss and Kolmer, Jour. Amer. Med. Assoc., 1922, **78**, 402.

[2] Jour. Amer. Med. Assoc., 1911, **56**, 492; Jour. Exp. Med., 1911, **14**, 196.

[3] See Voegtlin and Smith, Jour. Pharm. and Exp. Therap., 1920, **15**, 475; Nichols, Jour. Amer. Med. Assoc., 1921, **76**, 1335.

[4] See Schild, Dermat. Ztschr., 1902, **9**, 172; Lesser, Deutsch. med. Wchnschr., 1907, **33**, 1080; Koch, Ibid., 1890; Kopke, Bull de l'Acad. de Med., 1907, 3s., **58**, 64.

[5] See Roth, Reprint No. 688 from Pub. Health Rep., August 19, 1921.

[6] See "Preparation and Administration of Arsphenamine and Neoarsphenamine", Reprint No. 774 from Pub. Health Rep., August 4, 1922.

If precautions are taken to insure proper preparation of the solution, to exclude conditions of the patient which are contraindications to arsenical treatment, to prepare the patient properly before injection, and to inject the solution by the gravity method, reactions should be rare, although some cases may show even severe results due to possible idiosyncrasies or to the fact that the beginning dose was too large. Occasionally, following the first dose of arsphenamine even though everything has been carefully looked after, a reaction is observed known as the *Herxheimer reaction*, characterized by a rise in temperature, headache, nausea, malaise, and accentuation of the cutaneous symptoms. While such reactions may not be alarming in themselves, yet they are a warning that future treatment should be carefully carried out, and, if more severe reactions occur with succeeding injections, arsenical treatment should be discontinued.

Toxicity.—The toxic action of arsphenamine is potentially inherent in the compound itself, as there is sufficient arsenic present in the amount usually injected to produce severe and possibly fatal poisoning, provided conditions exist, either in the solution injected or in the patient himself, which result in the more or less prompt splitting off of the arsenic from its organic combination. At the present time the manufacture of arsphenamine is carefully regulated and each batch of the arsenical is scientifically tested, both chemically and biologically, by the methods laid down by the U. S. Public Health Service[1], in the effort to exclude products which may be toxic and which are the result of faulty manufacture[1]. However, these precautions can not prevent untoward results, which may arise from improper preparation of the solution used for injection or from careless manipulation by the physician. Thus, the official instructions for preparation of solutions of arsphenamine state that the distilled water used as solvent should be at room temperature, except where the product of the Dermatological Research Institute is used, in which latter case the water may be warm. Hunt[2] has found that some preparations of arsphenamine are very toxic when prepared at room temperature and that the toxicity is greatly reduced by gentle warming. However, the water should not be boiled, as has been done in some instances. Although *slight* shaking of the solution may be necessary to insure the redissolving of the precipitate formed on alkalinizing the original acid solution of arsphenamine, yet this should be reduced to a minimum, as Roth[3] and Schamberg, Kolmer and Raiziss[4] have shown that shaking such solutions in the presence of air increases the toxicity as determined on rats, while aeration was shown by Hunt[5] to increase the toxicity. A further source of possible trouble arises in the careless and improper alkalinization of the acid solution of arsphenamine[6], as insufficient alkali has often been added with the result that the monosodium salt is formed instead of the disodium compound, which is the one that should be used[7]. For proper results 0.85 cc. of normal sodium hydroxide solution should be added for each 0.1 gram of arsphenamine used. Another point, which is not infrequently overlooked, is that the filtered and diluted alkalinized arsphenamine solution should be allowed to stand for at least 30 minutes before being injected, in order to permit the completion of the chemical reactions and to reduce the toxicity of the solution as shown by Hunt[8] and Roth[9], although Ehrlich[10] reported that the toxicity of a solution of arsphenamine became 1½ times greater when the solution was allowed to stand exposed to the air for 4 hours. A further factor that must be borne in mind is the rate of injection of the solution. In no case should the rate exceed 25 cc. of solution in 1 minute or 4 minutes, and preferably 5, for a 0.4 gram dose. Should the patient show any sign of reaction, stop the injection at once.

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[1] Arsphenamine, as tested on white rats, should have a maximum tolerated dose value not below 120 mg. per kilo. See Roth, Bull. 135, Hyg. Lab. U. S. Pub. Health Service, March, 1924.

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[1] See Schamberg, Kolmer and Raiziss, Jour. Cutan. Dis., 1917, **35**, 286; Raiziss and Proskouriakoff, Arch. Dermat. and Syph., 1920, **2**, 280; Christiansen, Jour. Amer. Chem. Soc., 1920, **42**, 2402; Ibid., 1921, **43**, 370 and 2202; Raiziss and Gavron, Ibid., 582; Hooper, Kolls and Wright, Jour. Pharm. and Exp. Therap., 1921, **18**, 133; Oliver and Yamada, Ibid., 1922, **19**, 393.

[2] Jour. Amer. Med. Assoc., 1921, **76**, 854.

[3] Pub. Health Rep., 1921, **33**, 1990.

[4] Amer. Jour. Syph., 1922, **6**, 1.

[5] *Loc. cit.*

[6] Chambers, Jour. Amer. Med. Assoc., 1928, **91**, 320, advocates the addition of 2 drops of a 1 per cent. alcoholic solution of phenolphthalein to the arsphenamine solution in order to show that the solution used in the injection is really alkaline, as he believes this would aid in preventing accidents through the administration of acid arsphenamine solutions in mistake for those, which should have been alkalinized.

[7] Sodium arsphenamine, the salt formed by the alkalinization of the acid arsphenamine solution, is now available and, although not official, has been accepted for New and Non-official Remedies.

[8] Jour. Amer. Med. Assoc., 1921, **76**, 854.

[9] Pub. Health Reports, 1921, **36**, 1990.

[10] Abhandlungen über Salvarsan, 1913, **3**.

Martin[1] has classified the sequelae of arsphenamine injections as follows: (1) Slight untoward incidents in those whose tolerance is normal, such as vertigo, palpitations, nausea, and disturbances of taste and smell; (2) reactions in syndromes of discomfort and incapacity ascribed to allergy or acquired susceptibility, or to toxicity of the solution; (3) grave reactions, sometimes fatal, such as dermatitis exfoliativa, jaundice, hemorrhages, encephalitis, and gangrene; and (4) accidents, such as thrombosis, phlebitis, or infiltrations about the vein.

At the time of giving an intravenous injection or just after receiving it, the patient may show sudden angioneurotic symptoms such as pallor of the front part of the face followed by flushing, dyspnea, distress, cough, and precordial pain, and, occasionally, contractions of the muscles of the extremities, or the reaction may take the form of chills and fever. These immediate reactions, known as "nitritoid crises", are possibly physical, in contradistinction to the later reactions which are chemical in etiology, and have been ascribed to various causes such as precipitation of the drug in the circulating blood as believed by Danysz[2], to precipitation of protein compounds as advocated by Berman,[3] or to embolism as the result of agglutination of the red cells as put forth by Oliver and Yamada[4]. The purely physical factors do have some influence on the toxicity of arsphenamine solutions, as shown by the variation in toxicity of the acid solution as compared with the alkaline one, by the increasing of the toxicity on shaking and heating the solution, and the reduction in toxicity by standing[5]. It would be expected that the colloidal nature of arsphenamine might lead to a severe disturbance in the colloidal equilibrium of the blood[6], so that it is not suprising to find that there appears to be a close parallelism between the viscosity of arsphenamine solutions and their toxicity, as shown by Voegtlin, Johnson and Dyer[7].

There are, moreover, certain toxic effects following injection of arsphenamine, which are probably due to purely chemical factors. The symptoms of this action probably do not appear as quickly as those of the "nitritoid crises", although they may manifest themselves relatively soon. The patient may complain of a feeling of uneasiness and apprehension, malaise, headache, vertigo, disturbances in the sensation of taste and smell, nausea and vomiting, the latter possibly preceded by slight salivation and diarrhea. Rarely are the vaso-dilatory effects of the "nitritoid crises" noted, the blood pressure having a tendency to increase rather than to fall as it does in the latter conditions. These effects may pass off soon or they may become more intense and serious. These symptoms have been ascribed to the presence in the solution injected, or its formation soon after injection, of a partial oxidation product of arsphenamine, namely m-amino-p-hydroxyphenyl-arsenous oxide ($NH_2.OH.C_6H_3AsO$), usually called "arsenoxide". If the oxidation of the arsphenamine proceeds further to m-amino-p-hydroxyphenyl-arsenous acid, the toxicity of the solution is reduced, as has been shown by Hunt[1], and few if any symptoms will appear. Luithlen[2] believes that the early acute prostration, nausea and dysentery are attributable to the complex molecule acting as a whole and not to ionized arsenic, while the delayed effects are undoubtedly due to the dissociated arsenic, a conception accepted by Scott and Moore[3], who believe that toxic trivalent arsenic is liberated from the faultily eliminated arsphenamine. The serious effects following injections of arsphenamine are nephritis, jaundice with or without acute yellow atrophy[4], dermatitis exfoliativa, and encephalitis, while severe aplastic anemia has been reported after the arsphenamines by several.[5] Death may occur from any of these complications, or sudden collapse may follow the early symptoms. Burns and Bromberg[6] report fatal, multiple fat emboli in the brain, kidneys and lungs following injection of arsphenamine in a woman of 51 years of age.

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[1] Jour. Amer. Med. Assoc., 1920, **74**, 1218. See, also, Power, Jour. Roy. Army Med. Corps, 1927, **48**, 46.

[2] Ann. de l'Inst. Pasteur, 1917, **17**, 114. See, also, Berlin Letter, Jour. Amer. Med. Assoc., 1929, **92**, 489.

[3] Arch. Int. Med., 1918, **22**, 217. See, however, Schamberg, Kolmer, Raiziss and Weiss, Arch. Dermat. and Syph., 1920, **1**, 235; Schamberg, Tokuda and Kolmer, Ibid., 1921, **3**, 263.

[4] Proc. Soc. Exp. Biol. and Med., 1922, **19**, 304; Jour. Pharm. and Exp. Therap., 1922, **19**, 199. See, also, Oliver, Ibid., 393.

[5] See "Report of the Special Committee upon the Manufacture, Biological Testing, and Clinical Administration of Salvarsan and its Substitutes", No. 1, London, 1919.

[6] See Hunter and Patrick, Jour. Lab. and Clin. Med., 1925, **10**, 343 and 446.

[7] Reprint No. 898, Pub. Health Rep., Feb. 1, 1924.

It is impossible to give any reliable statistics as to the number of cases of poisoning following the administration of the organic arsenicals, as relatively few of those that occur find their way into the literature. It is probable that practically every physician, who makes extensive use of these compounds, has had some cases, possibly even fatal ones, so that the number of such cases would be very large were we able to correlate them. Luithlen[7] studied 274 fatalities from injections of arsphenamine, while Weiss[1] states that 29 deaths in New York City were attributed to arsphenamine from 1919 to 1925, but he adds that it is almost certain that more than this number have occurred.

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[1] Jour. Amer. Med. Assoc., 1921, **76,** 854.

[2] Ztschr. f. exp. Path. u. Ther., 1913, **13,** 495.

[3] Jour. Lab. and Clin. Med., 1928, **13,** 345.

[4] There seems to be some question as to the causative action of arsphenamine in the production of acute yellow atrophy, as this condition occurs in syphilis without administration of this drug. See Weiss, Jour. Amer. Med. Assoc., 1925, **84,** 577. The same thing is true of neoarsphenamine, although cases are reported, as for instance, Gordon and Feldman, Ibid., 1924, **83,** 1310.

[5] See Görke, Münch. med. Wchnschr., 1920, **67,** 1226; Moore and Foley, Arch. Dermat. and Syph., 1920, **1,** 25; Moore and Keidel, Ibid., 1921, **4,** 169; Dodd and Wilkinson, Jour. Amer. Med. Assoc., 1928, **90,** 663.

[6] Amer. Jour. Syph., 1930, **14,** 43.

[7] Ztschr. f. exp. Path. u. Therap., 1913, **13,** 495.

Distribution and Elimination.—The arsenical injected directly into the veins does not remain there for any length of time, as a very large part of it is promptly taken up by the tissues and stored therein, the liver, kidneys and spleen showing the largest amounts. Thus Willcox and Webster[2] found 0.0005 and 0.0003 gram of arsenic trioxide in 100 cc. of blood in two cases 1 hour after intravenous injection of 0.6 gram of arsphenamine, while Fordyce, Rosen and Myers[3] state that analysis of the blood taken immediately after completion of the injection showed that, in the case of arsphenamine, 60 per cent. of the arsenic injected has been localized outside of the blood stream, the maximum quantity of arsenic in the blood stream being found immediately after the injection to the extent of 4.21 mg. of metallic arsenic per 100 grams of dried blood; while with neoarsphenamine 62.1 per cent. of the arsenic is localized outside of the blood stream, the maximum quantity in the blood stream being 3.71 mg. of metallic arsenic per 100 grams of dried blood; and with silver arsphenamine 56.4 per cent. of the arsenic injected localizes outside of the blood stream, the maximum quantity in the blood stream being 2.62 mg. of metallic arsenic per 100 grams of dried blood. Their observations at later intervals up to 1 day indicate that the arsenic equilibrium, in the arsphenamine cases, gradually becomes lower, but that there is a marked increase in arsenic after a period of 1 day with a gradual diminution at later intervals; while with neoarsphenamine there is a gradual lowering of the arsenic content up to a period of 1 hour, when the amount becomes almost stationary. Underhill and Horn[4] show that, with increasing injections of neoarsphenamine into dogs, there is a slight but definite tendency toward a "lag" in the elimination of arsenic from the blood.

Inasmuch as there is a rapid disappearance of arsenic from the blood stream, it is to be expected that the urine would show the presence of arsenic in a very short time. The studies of Fordyce, Rosen and Myers[5] indicate that arsenic appears in the urine within 5 minutes after the injection, the initial value with arsphenamine being 5 mg. per 100 grams of dried specimen followed by a pronounced drop with a corresponding increase between the intervals of 1 and 6 hours; while with neoarsphenamine the high value for the excretion of arsenic was found at the interval of 1 hour and the initial excretion value in 5 minutes was about 3 times that of arsphenamine. From various researches it would appear that the largest amounts of arsenic are eliminated in the first 3 days following the injections and that the elimination is larger after the second and third doses than after the first. Weiss and Raiziss[1] state that only a small part of the arsenic derived from arsphenamine is eliminated through the urine, 13.5 per cent. being the highest amount in 14 days. While the excretion of the arsenic is only slight after the early days following the injection, yet it seems probable that traces may be found in the urine for some time, if very delicate methods of detection are used. Stümpke and Siegfried[2] claimed that traces of arsenic could be found in the urine of men several months after the injection, although Bailey and Mackay[3], in a study of 25 cases of delayed jaundice following arsphenamine, were unable to detect arsenic in the urine from 24 to 157 days after the last dose was given.

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[1] Jour. Amer. Med. Assoc., 1925, **84**, 577.

[2] Brit. Med. Jour., 1916, **1**, 473; The Analyst, 1916, **41**, 231.

[3] Amer. Jour. Syph., 1923, **7**, 225; Ibid., 528; Ibid., 1924, **8**, 34.

[4] Proc. Soc. Exp. Biol. and Med., 1927, **25**, 138.

[5] Amer. Jour. Syph., 1923, **7**, 209; Ibid., 1924, **8**, 619.

It is probable that the excretion of arsenic following arsphenamine is much greater through the feces than by the urine, Fraenkel-Heiden and Navassart[4] finding that the intestinal excretion was from 2 to 10 times greater than that through the kidney, and Underhill and Davis[5] reporting that as high as 53.76 per cent. of the arsenic injected is excreted in the feces in 1 week.

As is the case following administration of inorganic arsenic, much of the injected arsenic is stored up in the tissues, the liver, kidneys, spleen and muscles showing the highest amounts[6]. Where there have been several injections of the drug, the kidneys, at least in some cases as shown by Underhill and Dimick[7], may contain more arsenic than the liver, the latter organ showing little variation in amount of arsenic after repeated doses, owing, possibly, to the fact that arsenic is rapidly excreted into the intestines by the bile, Obregia and Carniol[8] detecting arsenic in the bile 25 minutes after intravenous injection of neoarsphenamine.

Neoarsphenamine.—This drug, introduced under the name of neosalvarsan ("914"), is a product obtained by the action of sodium methanal sulphoxylate on arsphenamine, and consists partially of sodium 3-3′ diamino 4-4′ dihydroxyarsenobenzene methanal sulphoxylate ($NH_2.OH.C_6H_3As{:}AsC_6H_3.OH.NH(CH_2O)OSNa$), and may consist of a di-substitution product or a mixture of the mono and di-substitution compounds. It contains not less than 19 per cent. of metallic arsenic. It is distributed, as is arsphenamine, only in sealed containers of colorless glass, from which the air has been excluded either by the production of a vacuum or by displacement with a nonoxidizing gas. It is a yellow powder, odorless or nearly so, and, in the dry state or in solution, is readily oxidized by exposure to air, becoming darker and more toxic. It is very soluble in water, soluble in glycerin, slightly soluble in alcohol and almost insoluble in acetone, chloroform and in ether. For tests of identity see the U. S. Pharmacopoeia.

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[1] Arch. Int. Med., 1922, **30**, 85. See, also, Ullmann, Arch. f. Dermat. u. Syph., 1912, **13**, 114 and 511; Lockemann, Biochem. Ztschr., 1916, **78**, 1; and Bergmann, Ibid., 1918, **90**, 348.

[2] Deutsche med. Wchnschr., 1911, **37**, 1793.

[3] Arch. Int. Med., 1920, **25**, 628.

[4] Ztschr. f. exp. Path. u. Therap., 1913, **13**, 531.

[5] Arch. Dermat. and Syph., 1922, **5**, 40.

[6] See Bornstein, Deutsche med. Wchnschr., 1911, **37**, 112; also, Fordyce, Rosen and Myers, Amer. Jour. Syph., 1924, **8**, 377.

[7] Amer. Jour. Physiol., 1928, **84**, 56.

[8] Compt. rend. Soc. de Biol., 1915, **78**, 468.

Neoarsphenamine is given in larger doses than is arsphenamine because it contains less arsenic and, ordinarily, is less toxic. The average dose is about 0.6 gram (9.3 grains), but, as a rule, the beginning dose should be small so that the patient's reaction may be determined. While the ratio of the minimal effective therapeutic dose to the lethal dose is 17 for arsphenamine, it is about 28 for neoarsphenamine. Although the toxicity of neoarsphenamine is, under ordinary circumstances, less than that of arsphenamine, as stated above, yet a very critical examination of the preparation itself and of the solution in water should be made before either is used, as neoarsphenamine occasionally decomposes in the ampule even when this is intact and always does so if the ampule is cracked and the powder is exposed to the air. The powder in the ampule should be freely mobile and lemon-yellow to canary-yellow in color. When it approaches a red color or is distinctly lumpy or solidified, the powder should not be used. In preparing the solution for injection 12.5 cc. of distilled water (at room temperature and never over 30° C.) should be used for each 0.1 gram of neoarsphenamine. The powder should be sprinkled on the water and allowed to go into solution with no agitation whatever, although slight rotation of the flask may be permissable, but the solution should not be shaken. In case this solution is not perfectly clear and transparent it should not be used under any circumstances, the time required for solution not being so important, providing this is not more than 10 minutes, as the complete solubility of the drug. Further, if the solution is dark in color it should not be used. In contradistinction to arsphenamine solutions, which are allowed to stand for 30 minutes before being used, solutions of neoarsphenamine should be used at once and in no case should they be allowed to stand for more than 20 minutes[1]. The drug is preferably administered by the gravity method of intravenous injection, the rate being about 0.1 gram in 30 seconds, which time is about ½ that required for arsphenamine. The same precautions as regards examination of the patient and his preparation for the treatment apply to neoarsphenamine as have been given for arsphenamine. In spite of all precautions severe and even fatal reactions occur from the administration of this drug, so that it must be used only with caution and only after one has had considerable experience with the preparation itself and with the possible reactions that may occur. As Roth[2] states: "It should be borne in mind that the margin of safety between the therapeutic and lethal dose of arsphenamine, for example, is extremely narrow in man as compared with certain other potent agents, and that this extremely narrow margin of safety of itself makes it necessary to regard arsphenamine as a potentially dangerous therapeutic agent, even though every precaution is taken to handle it properly."

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[1] See "Preparation and Administration of Arsphenamine and Neoarsphenamine", Reprint no. 774, Pub. Health Reports, August 4, 1922. See, also, Roth, Jour. Amer. Med. Assoc., 1922, 78, 1191.

[2] Reprint No. 688, Pub. Health Rep., Aug. 19, 1921. See, also, Roth, Pub. Health Rep., 1921, 36, 2523.

Toxicity.—The toxicity of neoarsphenamine is practically the same in quality as that of arsphenamine[1], differing only in degree and, possibly, in the lower frequency of severe reactions at the time of administration, although it must be remembered that solutions of neoarsphenamine, as well as the drug itself, have a tendency to decompose somewhat quicker than similar preparations of arsphenamine. Schamberg, Kolmer and Raiziss[2] have shown that the difference in toxicity between these arsenicals is proportionally greater than that of their arsenic content, some of this decrease in the case of neoarsphenamine possibly being due to the substitution in one or both of the easily oxidizable amino groups, although Roth[3] shows that the toxicity closely parallels the arsenic content, but that individual susceptibility is quite marked.

Silver Arsphenamine.—This is the sodium salt of silver-diamino-dihydroxy-arseno-benzene, the exact molecular formula of which has not been established. It contains approximately 20 per cent. of arsenic and 15 per cent. of silver. It is a brownish-black powder, unstable in the air. It is readily soluble in water, yielding a dark brown solution, which has an alkaline reaction.[4] The same rules for preparation apply as stated for arsphenamine, namely the solution should not be heated or shaken. After opening the ampule, the contents are sprinkled on the surface of 5 cc. of cool, sterile distilled water and sufficient cool sterile 0.4 per cent. sodium chloride solution is added so that the final solution approximates 20 cc. for each 0.1 gram of the drug. The solution must be administered promptly after its preparation. The usual dose is from 0.1 to 0.3 gram for adults.

"In the presence of organic diseases of the heart, aneurysm, aortitis, as well as in other parenchymatous diseased conditions of the glandular structures (liver and kidney), silver arsphenamine should be used only with great caution and in small doses, the patient and all functions being observed most carefully. If angioneurotic symptoms appear shortly after the injection, they should disappear rapidly; usually they may be avoided by the use of considerably diluted solutions. Susceptible individuals should not be treated during working hours. Hypersensitive patients should recline for some time after the injection. Argyria may occur rarely as a sequel to the use of the preparation."

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[1] Official regulations require that neoarsphenamine must have a maximum tolerated dose, as tested by tolerance of white rats, of at least 200 mg. per kilo.

[2] Amer. Jour. Med. Sci., 1920, **160**, 188. See, also, Raiziss and Falkov, Jour. Biol. Chem., 1921, **46**, 209.

[3] Bull. 113, U. S. Hyg. Lab., 1918.

[4] For tests of identity see *New and Nonofficial Remedies*, 1928, p. 78.

Although some workers believe that this compound has definite advantages over arsphenamine, others hold the opposite view[1]. From reports it would seem that immediate "nitritoid crises" are not common with this preparation, although some patients do show mild headache, chill, nausea, vomiting and some gastric disturbance[2]. Naegeli[3] reports that some lots of it induced some angioneurotic symptoms, while Corisa and Bejarano[4] state that it has a tendency to produce pain at the site of injection and, also, to form nodules and areas of infiltration. Occasional cases of periphlebitis and thrombosis have occurred.

According to the work of Fordyce, Rosen and Myers[5], 56.4 per cent. of the arsenic injected localizes outside of the blood stream, as shown by the analysis of blood taken immediately after the injection, the amount found in the blood being 2.62 mg. of metallic arsenic per 100 grams of dried blood. The maximum excretion of arsenic begins within 5 minutes after injection, as does than of arsphenamine, but the initial value is about 3 times that of arsphenamine, although the curve of excretion runs parallel to that of arsphenamine, as shown by Fordyce, Rosen and Myers[6]. As regards the localization of the arsenic in the tissues, following injection of silver arsphenamine, the same remarks apply as already made concerning arsphenamine and neoarsphenamine.

Sulpharsphenamine.—This arsenical was first prepared, or at least first fully described, by Voegtlin and Johnson[7], although there appears to have been a German patent (D.R.P.249726) issued in 1912 covering an arsenical of similar constitution but differing in many essential chemical, physical and biologic properties from the product elaborated by Voegtlin and Johnson. The product made by the process of the German patent was called sulfarsenol and has been studied by Levy-Bing, Lehnhoff-Wyld and Gerbay[8].

Sulpharsphenamine is disodium 3-3″ diamino-4-4″ dihydroxyarsenobenzene-N.dimethlyene sulphonate ($NaOSO_2CH_2NH.OH.C_6H_3As{:}AsC_6H_3OH.NHCH_2O_2SONa$) and contains not less than 19 per cent. of metallic arsenic but averaging 22 per cent. It is a light yellowish powder, which on exposure for days to moderately dry air does not change. It dissolves readily in cold water, forming a yellow to orange solution according to the concentration, the hydrogen ion concentration of a 1 per cent. solution varying between 3.2 and 4.6 and being, therefore, distinctly acid[1]. The drug yields the same qualitative tests as neoarsphenamine, from which sulpharsphenamine differs in having one additional atom of oxygen in each of the side chains attached to the NH group. A simple test to differentiate sulpharsphenamine from neoarsphenamine consists in treating the solutions with a few drops of an indigocarmine solution, which is decolorized by neoarsphenamine with the formation of a yellow solution, while sulpharsphenamine has no such action, although after reduction with zinc dust and acetic acid the filtrate from the sulpharsphenamine solution will then decolorize the indigocarmine solution.

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[1] See Rille and Frühwald, Münch. med. Wchnschr., 1919, **66,** 43; and Schlotz, Deutsche med. Wchnschr., 1920, **46,** 884.

[2] See Parounagian, Arch. Dermat. and Syph., 1921, **3,** 333.

[3] Schweiz. med. Wchnschr., 1920, **50,** 9.

[4] Arch. Dermat. and Syph., 1921, **3,** 465.

[5] Amer. Jour. Syph., 1923, **7,** 528. See, also, Ibid., 1924, **8,** 193.

[6] Amer. Jour. Syph., 1924, **8,** 377 and 619. See, also, Myers, Ibid., 1923, **7,** 125; Myers and Corbitt, Ibid., 1924, **8,** 704.

[7] Jour. Amer. Chem. Soc., 1922, **44,** 2573.

[8] Ann. des Mal. Vener., 1919, **14,** 520.

Sulpharsphenamine is administered in doses of from 0.4 to 0.6 gram and is as well tolerated, when injected intravenously, as is neoarsphenamine. Intramuscular injections of concentrated solutions cause some local reaction, which is, however, less severe than that following similar injections of arsphenamine or neoarsphenamine. For intramuscular or subcutaneous use the drug is dissolved in sterile, freshly distilled water in the proportion of about 0.1 gram to 0.3 cc.; while for intravenous use a greater dilution is desirable, about 0.1 gram to 2 to 3 cc.

The toxic dose of sulpharsphenamine for mice has been shown by Levy-Bing, Lehnhoff-Wyld and Gerbay[2] to be 400 mg. per kilo, while Voegtlin, Johnson and Dyer[3] report practically the same average value for intravenous injection in white rats, while by subcutaneous injection the average value is approximately 530 mg. per kilo. These workers give the maximum tolerated dose for rats as about 2/3 of the minimum lethal dose, or approximately 266 mg. per kilo, while Raiziss, Severac and Moetsch[4] state that "the most recent lots of sulpharsphenamine of whatever manufacture generally pass the standard toxicity tests at from 300 to 400 mg. per kilogram." It should be recalled, in this connection, that for rats the maximum tolerated dose of arsphenamine runs from 100 to 120 mg. per kilo, while that of neoarsphenamine averages 300 mg. per kilo, although some specimens run as high as 350 or 400 mg. per kilo. If, however, we use the trypanocidal power (minimum effective dose) of these 3 arsenicals as a test of their efficiency, employing the method of Voegtlin and Miller[5] in which the dose of the drug, which will sterilize the blood of rats infected with *trypanosoma equiperdum* within 24 to 72 hours, is taken as the minimum effective dose, the results seem to be somewhat different from those of the toxicity tests. Thus, with arsphenamine 4 mg. per kilo was generally sufficient to keep the animals free of parasites throughout the period of 7 days; with neoarsphenamine, equally consistent results were obtained with from 4 to 6 mg. per kilo, while, in the case of sulpharsphenamine, 14 to 18 mg. per kilo were required according to Raiziss, Severac and Moetsch[1] and Corbitt and Myers[2], while Voegtlin, Johnson and Dyer[3] obtained, as the average minimum effective dose, 22.8 mg. per kilo by the intravenous route and 25.3 when the drug was administered subcutaneously. On the basis of the chemotherapeutic index (the ratio of the maximum tolerated dose to the minimum effective dose) sulpharsphenamine, with an index of 22.2 is only slightly inferior to arsphenamine, whose index is 30, while it is only about ½ as efficient as neoarsphenamine with an index of 50, figures which agree closely with those of Fordyce, Rosen and Myers[4], who find that sulpharsphenamine is 2½ times less active therapeutically than neoarsphenamine.

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[1] Voegtlin, Johnson and Dyer, Pub. Health Rep., 1922, **37**, 2783.

[2] Ann. des Mal. Vener., 1919, **14**, 520.

[3] Pub. Health Rep., 1922, **37**, 2783.

[4] Jour. Amer. Med. Assoc., 1924, **83**, 1734.

[5] Pub. Health Rep., 1922, **37**, 1627.

It is generally recognized by clinicians that the chances for the complete cure of a generalized syphilitic infection, in which there is involvement of the central nervous system, are poor in many cases, possibly because the usual treatment with arsphenamine does not result in the penetration of the infected tissues by sufficient amounts of arsenic to destroy the last remaining parasites. As Voegtlin, Johnson and Dyer[5] remark: "After all, the main difficulty with the arsenicals in present use appears to consist in their failure to reach the last spirochetes which may be buried in lesions that are difficultly accessible. It is obvious that incomplete sterilization of the patient due to this cause will prevent a cure and will cause, sooner or later, clinical replases." This same idea is expressed a little differently by Raiziss[6], when he says, "In almost 20 per cent of the cases of treated syphilis, the positive Wassermann reaction cannot be rendered negative. Furthermore, in a considerable number of apparently Wassermann negative cases complete cure has not been achieved."

By a combination of chemical and biological methods of study, in which the amount of arsenic in the spinal fluid and brain tissue of rabbits following intravenous injection of the arsenicals was determined and the sterilizing influence of intravenous injection of the arsenicals upon trypanosomes injected into the cranial subarachnoid space of rabbits was investigated by the method of Smith and Voegtlin[7], it has been found by Voegtlin, Dyer and Thompson[8] that arsphenamine, neoarsphenamine, and silver arsphenamine have a relatively low effectiveness, while sulpharsphenamine is the most effective arsenobenzene derivative, comparing favorably with the highly effective tryparsamide (a pentavalent aromatic arsenical), and would seem to be especially indicated in treatment of cases of neurosyphilis, although Fordyce, Rosen and Myers[1] could not show that sulpharsphenamine had any special affinity for the central nervous system. By means of experiments upon rabbits inoculated with syphilis, using a modification of the tissue transfer method of Pearce and Brown[2], it was found by Voegtlin and Dyer[3] that the maximum tolerated dose of arsphenamine for rabbits was 63 mg. per kilo, of neoarsphenamine 163 mg. per kilo, and of sulpharsphenamine 208 mg. per kilo, while the minimal sterilizing dose (the dose which causes the rapid disappearance of the spirochetes from the primary lesions and the healing of the lesions) is the same in terms of amount of arsenic used for all 3 of these arsenicals, but in terms of mg. of drug per kilo of weight of rabbit is 23.5 for arsphenamine, 40 for neoarsphenamine, and 35 for sulpharsphenamine, thus yielding an index of sterilization (ratio of maximal tolerated dose to minimal sterilizing dose) of 2.7, 4 and 6 respectively. Judged from these two viewpoints (1) of relative penetrative power into the spinal fluid and nerve tissues and (2) of actual index of sterilization, sulpharsphenamine would seem to be a more effective drug than either arsphenamine or neoarsphenamine, especially in the treatment of parenchymatous neurosyphilis. However, if this sterilizing dose, as given above, is compared with the maximum tolerated dose for man of 10 mg. per kilo for arsphenamine, 15 mg. for neoarsphenamine, and 10 mg. for sulpharsphenamine, it is obvious that the minimum sterilizing doses for rabbits far exceed the maximum doses which can be used clinically[4]. As even prolonged treatment does not effect sterilization of the human in a large number of cases at least, Voegtlin and Dyer have suggested the combination of sodium thiosulphate with arsphenamine, neoarsphenamine, or sulpharsphenamine as a means of intensifying the action of these compounds without increasing the toxicity of the larger doses to be given or without decreasing the parasiticidal effect of the drug. The sodium thiosulphate may be given either by separate intravenous injection at the time of the arsenical treatment or orally before breakfast and the arsenical given during the forenoon.

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[1] Jour. Amer. Med. Assoc., 1924, **83**, 1734.

[2] Jour. Amer. Pharm. Assoc., 1923, **12**, 1068.

[3] Pub. Health Rep., 1922, **37**, 2783.

[4] Amer. Jour. Syph., 1925, **9**, 18.

[5] Pub. Health Rep., 1922, **37**, 2783. See, also, Engelmann, Arch. f. exp. Path. u. Pharm., 1928, **133**, 181.

[6] Amer. Jour. Syph., 1927, **11**, 517.

[7] Jour. Pharm. and Exp. Therap., 1921, **17**, 342.

[8] Pub. Health Rep., 1923, **38**, 1003.

Treatment.—The treatment of the "nitritoid crises" should be directed toward the control of the vasomotor disturbances. The pulmonary effects should be treated by placing the patient in a sitting posture and administering hypodermically either 1 cc. of 1:1000 solution of adrenalin hydrochloride or $\frac{1}{50}$ grain of atropine, while the cardiac symptoms should be handled by placing the patient in the recumbent position and giving strychnine hypodermically.

For the jaundice and dermititis, intravenous or oral administration of sodium thiosulphate, as discussed on page 449, should be pushed. This treatment is especially effective and seems to have few if any untoward effects, although Frazier[1] reports 3 cases of arsphenamine dermatitis in which the treatment was said to have aggravated the skin lesions. According to Power[2] the liver complications may be prevented by administering by the mouth a mixture of glucose and sodium bicarbonate ½ hour prior to the injection, on the theory that this causes the filling of the liver cells with glycogen and that such cells have a lessened affinity for arsenic. Further treatment should be symptomatic.

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[1] Amer. Jour. Syph., 1925, **9,** 18.

[2] Jour. Exp. Med., 1922, **35,** 39.

[3] Pub. Health Rep., 1927, **42,** 176.

[4] Voegtlin and Dyer, Ibid., 1045.

Pentavalent Organic Arsenicals.—The pentavalent organic arsenicals are less toxic than those of the trivalent series just discussed and they are, also, less effective therapeutically than the trivalent compounds. Many of these pentavalent compounds have been used in the past, but, as shown on page 519, some of these at least do not exercise sufficient spirocheticidal or trypanocidal affects to warrant their use, especially when the trivalent compounds are available.

Sodium Cacodylate.—This salt of cacodylic acid (which, in turn, is dimethyl arsonic acid) is still official and contains not less than 72 and not more than 75 per cent of $(CH_3)_2AsO.ONa$ with variable amounts of water. It occurs in white prisms or as a white granular powder, which is odorless and deliquescent, and very soluble in water and alcohol. In the anhydrous state it contains 46.84 per cent. of metallic arsenic.[3] Its use in spirochetal infections has practically been discontinued at the present time, although it is occasionally used as a general tonic in doses ranging from 0.02 to 0.12 gram (⅓ to 2 grains) given subsutaneously, its therapeutic action depending upon the slow but continuous dissociation of the arsenic according to Heffter. While this drug ordinarily does not exert severe toxic effects, yet Lebahn[4] has shown that it will produce death in rabbits in 4 to 5 days following a dose of 0.25 gram, a finding confirmed by Schulz[5] and Rabuteau[6]. The symptoms of poisoning from this drug are practically those of a mild arsenical poisoning, Lafon[7] reporting a case in which there were edema of the lids, nausea, gastric pain, dryness of the throat, great thirst, and pains in the head and limbs. However, doses as large as 2 grams have been taken without harm[8]. Ordinary doses of the drug are eliminated by the urine unchanged, the elimination beginning soon and continuing for as long as 30 days; while after repeated doses or single large doses, a part of the arsenic is eliminated by the urine in the inorganic form, some also appearing in the feces, while Dawes and Jackson[9] showed that the tissues contained inorganic arsenic.

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[1] Jour. Amer. Med. Assoc., 1927, **88**, 537.

[2] Jour. Royal Army Med. Corps. 1927, **48**, 46.

[3] For tests of identity see U. S. Pharmacopoeia, 10th rev., 1925, p. 339.

[4] Dissertation, Rostock, 1868. Cited by Witthaus, *Toxicology*, 1911, p. 588.

[5] Arch. f. exp. Path. u. Pharm., 1879, **11**, 131.

[6] Compt. rend. Soc. de Biol., 1882, 7 s., **4**, 491.

[7] Gaz. hebdom. de sc. med. de Bordeaux, 1903, **24**, 273.

[8] Bayeux, Rev. int. de méd. et de chir., 1906, p. 54.

[9] Jour. Amer. Med. Assoc., 1907, **48**, 2090.

Arrhenal.—This arsenical, also known as neo-arsykodile and arsynal, contains one methyl group less than cacodylic acid and is disodium-methyl-arsonate ($CH_3AsO.(ONa)_2$). When crystallized with 6 molecules of water it contains 25.68 per cent. of metallic arsenic. It is a white, odorless, water-soluble crystalline substance. It is used in doses of 0.1 gram (1½ grains) for the same purposes as is sodium cacodylate, but it has little effect on the spirochetal infections. Its toxicity is about the same as that of sodium cacodylate, doses of 1 gram having been followed by vomiting and diarrhea, but with no epigastric pain[1].

Atoxyl.—This is the sodium salt of arsanilic acid (p-amino-phenyl-arsonic acid, $C_6H_4NH_2AsO.OH.ONa$) and crystallizes with varying amounts of water. When anhydrous it contains 31.36 per cent. of metallic arsenic. It is a white, odorless, water-soluble crystalline substance. It is especially valuable in the treatment of sleeping sickness and is given hypodermically in doses of 0.02 to 0.2 gram (⅓ to 3 grains) every other day, increasing to single doses of 0.65 gram (10 grains). The toxicity of atoxyl appears to be intermediate between that of the inorganic arsenicals and that of the cacodylates. The symptoms of this toxic action have been variable, being characterized, according to the summary of reported cases as cited by Witthaus[2], by depression, chilly sensations, insomnia, occasionally somnolence, attacks of vertigo and syncope, fever, dryness and a sensation of scratching in the throat, coughing, dyspnea, slowing of the pulse, angina pectoris, anorexia, eructations, vomiting, sometimes of blood, colic, abdominal cramps, diarrhea, occasionally icterus, retention of urine with strangury and albuminuria, various exanthemata, cold extremities and paresthesias in the legs. Its most dangerous action is, however, directed toward the visual organs, causing retinal hemorrhages, optic nerve atrophy, amaurosis, and permanent blindness. On account of which action its use has been practically discontinued, except in sleeping sickness, for which it seems to be almost specific. In the fatal case reported by Schlecht[3], in which a man received 2.4 grams in 4 hypodermic injections within 8 days, death occurred on the second day after the last injection from pulmonary edema, the symptoms of a severe attack of the paralytic form of acute arsenical poisoning being manifested.

Atoxyl is largely eliminated by the urine in the unchanged form, but some is also excreted by the feces. The urinary elimination begins rather rapidly and is very active during the first 24 hours, while it may be prolonged for days. In his experiments on dogs, Simonet[4] found in the organs of a dog the following amounts of arsenic in mgs. per kilo: bile 64; kidney 50; lungs 40; liver 36; blood 36; spleen 6.5; muscles 5; brain 4; and hair 3.

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[1] LeRoy des Barres, Arch. gén. de méd., 1903, **1**, 1635.

[2] *Toxicology*, 1911, p. 591.

[3] Münch. med. Wchnschr., 1909, **56**, 972.

[4] Bull. Soc. pharm., Bordeaux, 1908, **20**, 443.

Arsacetin.—This is the sodium salt of acetyl arsanilic acid (p-acetyl-amino-phenyl-arsonic acid, $CH_3CONHC_6H_4AsO.OH.ONa$). As Raiziss, Schamberg and Kolmer[1] have shown, the toxicity as well as the curative power of organic arsenicals depend somewhat upon the nature of the amino group or groups, that is whether they are free or substituted, the general tendency being for the substituted products to be less toxic and, at the same time, to have less therapeutic effect, although in some cases the toxicity may be increased, while in others it may remain the same or be diminished, while the therapeutic effect is increased. Arsacetin crystallizes with 5 molecules of water of crystallization in the form of fine white needles easily soluble in water and in methyl alcohol, and is odorless and tasteless. It contains when anhydrous 26.67 per cent. of metallic arsenic. Its toxicity is much less than that of atoxyl.

Acetarsone.—This arsenical, also known as *Stovarsol*, is 3-acetylamino-4-hydroxyphenyl-arsonic acid ($CH_3CONH.OH.C_6H_3AsO.(OH)_2$). It is a white, odorless powder, having a slightly acid taste. It is slightly soluble in water and alcohol; readily soluble in solutions of alkalies or alkaline carbonates. It is stable at ordinary temperatures and contains from 27.1 to 27.4 per cent. of metallic arsenic[2].

This drug is therapeutically less effective than arsphenamine in syphilis, although it apparently has some value as a prophylactic in this disease[3], as claimed by Levaditi[4], Oppenheim[5], and Poole[6], the drug being given orally in doses of 1 gram on 3 successive days. It is claimed to yield satisfactory results in the eradication of dysenteriae cysts and encysted flaggelates, and in the treatment of general amebic dysentery and malaria[7], when administered orally in doses of 0.25 gram three times daily for a period of seven days. Acetarsone is not, however, without some toxic effects, as it may produce malaise, fever, edema, jaundice, diarrhea, albuminuria, bronchitis, and such skin manifestations as urticaria and erythema, while exfoliative dermatitis may occur in some cases.[8] Anderson and Leake[9] show that the minimum lethal dose of acetarsone administered orally to cuts and rabbits is between 125 and 175 mg. per kilogram.

Tryparsamide.—This pentavalent arsenical, first prepared by Jacobs and Heidelberger[10], is, also, a derivative of arsanilic acid in which acetamide is introduced into the amino group. It is sodium-N-phenylglycinamide-p-arsonate ($NH_2COCH_2NH.C_6H_4AsO.OH.ONA$) and contains 24.6 per cent. of arsenic. It occurs as a colorless, odorless, crystalline powder, freely soluble in water, forming a solution neutral to litmus. It is insoluble or only slightly soluble in alcohol, ether, chloroform, and benzene[1]. It may be administered subcutaneously, intramuscularly, or intravenously, the latter being preferable, but it should never be given orally. In general the dose should not exceed 0.04 to 0.05 gram per kilo of body weight and such doses should not be repeated at intervals of less than 1 week.

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[1] Proc. Soc. Exp. Bio. and Med., 1921, **18,** 149.

[2] For tests of identity see *New and Nonofficial Remedies*, 1928, p. 84.

[3] See Levaditi, Navarro-Martin, Fournier, Guénot, and Schwartz, Ann. de l'Inst. Pasteur, 1922, **36,** 729.

[4] Bull. Soc. Franc. de Dermat. et de Syph., 1924, p. 513.

[5] Wien. klin. Wchnschr., 1926, **39,** 627.

[6] Bull. Johns Hopk. Hosp., 1926, **38,** 242.

[7] See Petzetakis, Presse méd., 1925, **33,** 299; and Marchoux and Cohen, Compt. rend. Soc. de Biol., 1925, **92,** 132.

[8] See Michael, Jour. Amer. Med. Assoc., 1929, **92,** 645.

[9] *Proc. Soc. Exp. Bive. and Med.,* 1930, **27,** 267.

[10] Jour. Amer. Chem. Soc., 1919, **41,** 1589 and 1602.

Tryparsamide is primarily a trypanocidal agent and has been recommended in the treatment of certain forms of trypanosomiasis, such as African sleeping sickness. In the case of human trypanosomiasis due to *T. gambiense*, it is relatively easy to sterilize the peripheral blood by a single dose of the drug, but relapses may occur unless the treatment is continued for some time[2], single doses of from 0.5 to 5.0 grams producing a peripheral sterilization of lymph glands and blood in an average of 6 to 12 hours. Pearce found that the duration of the peripheral sterilization following single doses of 17 to 83 mg. per kilo ranged from 17 to 58 days in patients, who ultimately showed a return of trypanosomes to the peripheral blood, although a number of patients showed no such relapse in periods ranging from 40 to 111 days. She reports that the immediate trypanocidal action after intramuscular administration was as rapid as that following the intravenous route, while the duration of peripheral sterilization was appreciably longer. As shown by Raiziss, Severac and Moetsch[3], the maximum tolerated dose of tryparsamide for rats is 1.8 gram, its trypanocidal effect being only about ½ that of arsanilic acid.

Tryparsamide has some spirocheticidal activity, but its curative affect in experimental rabbit syphilis is low. However, it appears to have an unusual power of penetration into the cerebrospinal fluid and nerve tissues, as shown by Voegtlin, Smith, Dyer and Thompson[4], although Fordyce, Rosen and Myers[5] and Schrenk[6] failed to show any significant difference in the arsenic content of nervous tissues of animals following intravenous administration of tryparsamide and the arsphenamines. Clinically, the best results from tryparsamide seem to have been obtained in patients suffering with neurosyphilis and especially with early paresis, as shown by Lorenz, Loevenhart, Bleckwenn, and

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[1] For tests of identity see *New and Nonofficial Remedies*, 1928, p. 88.

[2] See Brown and Pearce, Jour. Exp. Med., 1919, **30**, 417; Pearce and Brown, Ibid., 437 and 455; Brown and Pearce, Ibid., 483; Pearce and Brown, Ibid., 1921, **33**, 193; Pearce, Ibid., 1921 (supplement), **34**, 1.

[3] Trans. Sect. on Pharmacol. and Therap., Amer. Med. Assoc., 1925, p. 66.

[4] Pub. Health Rep., 1923, **38**, 1003.

[5] Amer. Jour. Syph., 1924, **8**, 34; Ibid., 1925, **9**, 490.

[6] Cited by Loevenhart and Stratman-Thomas, Jour. Pharm. and Exp. Ther., 1926, **29**, 69.

Hodges[1], of the group of cases studied approximately 50 per cent. recovering mentally, their improvement being, in most cases, prompt and outspoken. Loevenhart and Stratman-Thomas[2] believe that the action of tryparsamide is not to be explained primarily on the basis of its spirocheticidal action, but that in some manner it modifies the response of the tissues to the presence of the spirochetes, with the result that there is a resorption of the inflammatory infiltration and a consequent improvement in the nutrition of the cells. In tabetic cases the response to tryparsamide is less satisfactory, the drug occasionally hastening the progress of the disease.

The toxic effects of tryparsamide are similar to those of the other pentavalent arsenicals, especially prominent being the tendency to amblyopia and, occasionally, jaundice. "Before using the drug, careful consideration should be given to the frequent production of visual injury, which may be serious and permanent. This caution is especially important if the neurosyphilis has involved the optic nerve."

Detection of Organic Arsenicals.—Owing to the fact that the organic arsenicals are eliminated, as a rule, somewhat less readily and, as a consequence, that the elimination may continue for a longer time, the various organs submitted for toxicological examination may contain varying amounts of arsenic in the organic form as a result of the therapeutic use of these drugs. For this reason, it is wise for the analyst to acquaint himself with the possibilities of the case, before he draws definite conclusions as to the actual presence of a case of arsenic poisoning. When one remembers that a dose of arsphenamine, for instance, may yield to the tissues between 2 and 3 grains of metallic arsenic, it is essential to ascertain, if possible, whether the arsenic found in his examinations may not have come from the therapeutic use of such arsenicals rather than from the administration of arsenic with homicidal intent. While it is doubtful that the relatively large amounts commonly found in the tissues in true acute poisoning could be traceable to the residues from therapeutic use, yet, after repeated doses of these organic arsenicals, appreciable amounts may be found in the tissues, the figures being about of the same magnitude as those found in cases of delayed death from true inorganic arsenic poisoning. In such cases it is important to determine whether arsenic can be found in the stomach contents or feces, and, especially, whether the organic arsenical as such is present in the urine. However, even the urine may show no trace of the organic arsenic at the time of the examination, although the tissues still contain residues from such source.

The organic arsenicals do not, as a general thing, respond to the usual tests for inorganic arsenic, although some of them yield certain of these tests. However, if the tissues be completely oxidized by special methods to be mentioned later, these arsenicals will give the tests for arsenic acid, but the usual methods of extraction will not ordinarily effect the desired results.

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[1] Jour. Amer. Med. Assoc., 1923, **80**, 1497.

[2] Jour. Pharm. and Exp. Ther., 1926, **29**, 69. See, also, Lorenz, Loevenhart, Reitz and Eck, Amer. Jour. Med. Sci., 1924, **168**, 157.

To detect the presence of the organic arsenical in the tissues proceed as follows, using the method of Vitali[1]. Mix the finely divided tissue with water, acidify with tartaric or hydrochloric acid, and evaporate to dryness. Extract this residue 2 or 3 times with hot 90 per cent. alcohol on the water-bath, filter, distill off the alcohol from the filtrate, and treat the syrupy residue with absolute alcohol, stirring thoroughly to insure complete solution of the arsenical and precipitation of foreign material. Filter and evaporate off the alcohol. Take up the residue with water and examine qualitatively as follows.[2]

1. Test a portion of the filtrate by means of the Reinsch, Marsh, or Gutzeit tests. Positive tests will be given by the arsphenamines, atoxyl, arsacetin and other arsanilic acid compounds, but not by the cacodylates. If inorganic arsenic is present in the tissues, some of it will be extracted by the above process and will, of course, yield the tests mentioned.

2. Test a further portion of the filtrate with Bettendorff's reagent[3], using 3 parts of the reagent to 1 part of the filtrate, and warm. In the presence of inorganic arsenic a brown color or a brownish-black precipitate will be formed, while with the organic arsenicals no brownish or black color will be observed, but a lemon-yellow color or precipitate may be noted.

3. Test a further portion of the filtrate with the diazo raction[4]. This is, in reality, a test for a primary aromatic amine and, as such, is not characteristic of the arsenicals without further proof. After diazotizing, the diazonium salts will form dyes with such phenolic compounds as resorcinol, phloroglucinol, orcinol, α-naphthol, β-naphthol, and α- and β-naphthlamine[5]. Acidify the filtrate with a few drops of hydrochloric acid, cool in ice water, and add a few drops of a 0.5 per cent. solution of sodium nitrite and gradually add this mixture to a solution of 0.3 gram of resorcinol in about 5 cc. of water to which 2 or 3 cc. of 20 per cent. sodium carbonate solution have been added, warming slightly to accelerate the reaction. In the presence of arsphenamine the resorcinol solution will produce a red color, while if atoxyl be present the color is more of a purplish-red. Instead of using resorcinol, an acidified saturated solution of α- or β-naphthylamine may be employed, the colorations

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[1] Boll. Chim. Farmacol., 1901, **40**, 657; 1903, **42**, 641.

[2] For tests of identity see *U. S. Pharmacopoeia*, 10th Rev., 1925 and *New and Nonofficial Remedies*, 1928. See, also, Gadamer, *Lehrbuch der chemischen Toxikologie*, 2te. Aufl, 1924, p. 180 et seq.

[3] Ztschr. f. Chem., 1869, 2R., **5**, 492. This reagent consists of a solution of 1 part of crystallized stannous chloride in 3 or 4 parts of concentrated HCl.

[4] See Ehrlich and Bertheim, Ber. d. d. chem. Ges., 1907, **40**, 3292.

[5] Although the tests with the naphthylamines are more sensitive, yet they are less reliable and less characteristic than those with the other phenols.

being somewhat more violet in tone under these circumstances. Atoxyl may be distinguished from arsphenamine by the formation of an azo-dye with α-naphthylamine, while arsphenamine gives no such dye, although both form dyes with α-napthylamine. Should the naphthylamines be used in this test, it is necessary to remove the excess of nitrous acid by gradual addition of urea solution[1] (as these bases themselves have a tendency to form colorations by partial autodiazotizing), the urea solution being added until a drop of the solution no longer gives a blue color with starch-iodide paper. As the mere formation of these dyes is not conclusive of the presence of arsenic, saturate the colored solution with NaCl and allow the mixture to stand for several hours. Filter off the precipitated dye, wash with saturated salt solution, dissolve in hot dilute HCl and test for arsenic by the Reinsch or Gutzeit tests.

Determination.—Extract the finely divided, weighed tissue by the method of Vitali as discussed on page 538, transfer the watery extract to a 200 cc. glass-stoppered flask and evaporate to a thick syrup. Then apply the method of Lehmann[2] as follows. Add 1 gram of finely powdered potassium permanganate and 5 cc. of diluted sulphuric acid, and allow to stand for 10 minutes, rotating the contents of the flask during this time to insure thorough mixing. Add 10 cc. of concentrated sulphuric acid in portions of about 2 cc., rotating the flask after each addition. When the reaction has ceased, add sufficient hydrogen dioxide solution to dissolve completely the brown precipitate (about 5 to 7 cc.). Toward the end of the reaction the hydrogen dioxide is to be added drop by drop to avoid any great excess. Dilute with 25 cc. of distilled water, and boil gently over an asbestos wire gauze for from 15 to 20 minutes, or until the excess of hydrogen dioxide is expelled. Dilute with 50 cc. of distilled water, and add N/10 potassium permanganate until the liquid is faintly pink, then discharge the pink color by the addition of a drop of N/10 oxalic acid. Cool the solution, add 2.5 grams of potassium iodide, stopper the flask tightly, and allow it to stand in a cool, dark place for 1 hour. Then titrate the liberated iodine with N/10 sodium thiosulphate without the use of the starch indicator. Make a blank test with the same quantities of the reagents, and correct the determination for the volume of N/10 sodium thiosulphate used in the blank. Each cc. of N/10 sodium thiosulphate corresponds to 0.003748 gram of arsenic.

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[1] As urine contains enough urea to take care of the excess of nitrous acid, this test may be applied directly to the urine. See Abelin, Münch. med. Wchnschr., 1911, **58,** 1002.

[2] Apoth. Ztg., 1912, **27,** 545. See, also, Myers and Dumez, Pub. Health Rep., 1918, **33,** 1003. Instead of this method, one may employ that of Rogers, Can. Chem. Jour., 1920, **3,** 398 or that of Robertson, Jour. Amer. Chem. Soc., 1921, **43,** 182. In their work Fordyce, Rosen and Myers, Amer. Jour. Med. Sci., 1922, **164,** 492, dried the specimens, decomposed with nitric and sulphuric acid, evaporated to dryness and fused the residue with sodium nitrate, determining the arsenic in the sulphuric acid solution by the Marsh test.

ANTIMONY

Antimony is found but rarely in its native state, although the sulphide and oxide are rather wide-spread, while it not infrequently is found in nickel, copper, lead and silver ores. In times past it has been rather extensively used in medicine, but, at present, its employment in therapeutics is almost entirely limited to emetic preparations. In the arts antimony compounds find some usage, the sulphide being used in percussion caps, in red and blue fires and in the heads of some Swedish matches, while sulphurated antimony (a mixture of the sulphide and oxide) is employed in the vulcanization of rubber, which it colors red-brown. The trichloride (butter of antimony) is employed as a bronzing liquid, in farriery, and occasionally as an external application or escharotic.

Antimonial poisoning has occurred from inhalation of antimonial fumes by operatives in smelting plants or by workers with the sulphide[1] and subtle unsuspected antimony poisoning may arise in children from the presence of antimony in the red rubber nipples used on milk bottles[2]. Further, acid vegetables and fruits may extract some antimony from certain grades of enamelled cooking utensils, as shown by Miller[3]. Although antimony trioxide has been responsible for a few cases of poisoning[4], practically all reported cases are due to the trichloride or to tartar emetic. According to Witthaus[5] the literature reveals records of 10 cases of poisoning by the trichloride, 4 were accidental, 4 suicidal, and in 2 it was "taken by" the patient; while the same authority states that, of 124 cases of poisoning with tartar emetic, 89 were accidental, 6 suicidal, 20 homicidal and 9 uncertain.

At the present time the only official compound of antimony is *Antimonii et Potassii Tartras* ($K(SbO)C_4H_4O_6$, antimonyl potassium tartrate, tartrated antimony, tartar emetic). This occurs in the form of colorless, odorless, transparent crystals of the rhombic system, or as a white granular powder, the crystals being efflorescent in the air. It is readily soluble in water and glycerin but insoluble in alcohol. This compound is found, also, as a constituent of *mistura glycyrrhizae composita* and of *syrupus scillae compositus.* Recently certain organic antimonials have been introduced for the treatment of such trypanosomal infections as kala azar and filiariasis, and the results obtained in experimental work by Rowntree and Abel[6] and by Randall[7] with antimony thioglycollamide and antimony sodium thioglycollate would seem to justify their use.

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[1] See Hamilton, Chem. Trade Jour., 1919, **65**, 365.

[2] See Bull 96, Hyg. Lab., 1914, p. 56.

[3] Jour. Home Econ., 1916, **8**. 361.

[4] See Page, Lancet, 1879, **1**, 699.

[5] *Toxicology*, 1911, p. 351.

[6] Jour. Pharm. and Exp. Ther., 1910, **2**, 101.

[7] Jour. Urol., 1923, **9**, 491; Amer. Jour. Med. Sci., 1924, **168**, 728.

Symptoms.—The symptoms following the ingestion of the chloride are to a large extent those of a severe gastro-intestinal irritant and corrosive, its action being comparable to that of strong hydrochloric acid, although some phases of the action may be traceable to the antimony.

With tartar emetic, we find some resemblance to the action of arsenical compounds, although the action is by no means identical. As Schmiedeberg[1] has shown antimony has a stronger local action, due, probably, to the fact that the compounds are relatively more difficultly absorbable than are the arsenicals. In a very short time there is an acrid and metallic taste in the mouth, followed by a sense of constriction of the throat and esophagus, salivation, marked expectoration, nausea, and, in a few minutes (10 to 30), almost uncontrollable vomiting, pain in the stomach and abdomen, diarrhea with cholera-like watery stools, sometimes involuntary and sometimes attended with tenesmus, coldness of the skin, fainting attacks and depression, associated with a rapid pulse, which later becomes weak, as does the respiration. Later follow vertigo, unconsciousness, spasmodic contractions of various groups of muscles or general convulsions, collapse and death. In these cases, even though the severity of the symptoms, characterized by excessive vomiting and collapse and depression, would seem to indicate a serious outcome, yet there is a remarkable tendency to recover. Usually, the vomiting is so excessive that most of the antimonial is ejected and very little absorbed, so that acute antimony poisoning differs from acute arsenical poisoning in this respect. Even when there has been practically no vomiting following large doses, recovery may follow, as in the case cited by Taylor[2] of recovery following a dose of 240 grains, the patient vomiting only once and that 1/2 hour after swallowing the poison. If, however, a second dose is given about the time when the patient is recovering from the former dose, the resulting depression will usually be fatal.

In the *chronic type of poisoning* following the administration of repeated small doses of tartar emetic, the patient has a loathing for food, because if taken it is almost immediately vomited, suffers from pain in the stomach and bowels, diarrhea, physical and nervous weakness, muscular cramps, weak pulse and cold sweats. The person becomes emaciated, the eyes appear sunken and watery, the face is flushed, the cheeks become hollow, and death finally results from exhaustion.

Distribution and Elimination.—Owing to the almost persistent vomiting and purging following intake of tartar emetic, a large part of that ingested is lost in this way. That antimony is absorbed to a certain extent is shown by its excretion through the urine. In some cases this is very rapid, Wormley[3] citing some experimental work of Hock showing that, following the intake of 10 mg. of antimony in solution, this metal was found in the urine within 5 minutes in 1 case and, in several instances, within 10 to 15 minutes, the greatest elimination taking place within 1 to 2 hours and then gradually diminishing, although traces were still present as late as 96 hours after the dose was taken. Millon and Laveran[1] found that there were intermissions in this elimination when the urine showed no antimony, but that, in some cases, antimony was present in the urine from 15 to 24 days after the last administration.

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[1] See Kobert, *Lehrbuch der Intoxikationen*, 1906, **2**, 278.

[2] *On Poisons*, 3rd Amer. Ed., 1875, p. 443.

[3] *Micro-Chemistry of Poisons*, 2nd ed., 1885, p. 237.

Following intravenous or subcutaneous injection of antimony salts, this metal may be found in the stomach and intestines, so that the gastrointestinal tract plays a role in the elimination of antimony.

After absorption antimony is stored up in the liver and other organs, just as is the case with arsenic. Although there is large loss of antimony through the stomach and bowels after large doses, yet some is absorbed and must find its way to the liver. Chapuis[2] believed that the liver will not contain antimony if death results rapidly from a single large dose, but experiments on animals by Orfila[3] show that antimony in large amounts was found in the liver and kidneys after death from single large doses. Just how long a period must elapse before the stored antimony is entirely eliminated is unknown, but it has been shown by Millon and Laveran[4] that the liver and bones of dogs killed 3½ and 4 months after the last dose of tartar emetic contained antimony in appreciable amounts, while a patient of theirs, who died from tuberculosis 24 days after the last dose of tartar emetic, showed antimony in the liver. The brain, also, has a tendency to absorb and retain antimony, as shown in the case of Stevenson[5] and in the experimental work of Chittenden and Blake[6].

Fatal Dose.—It seems to be a peculiarity of antimony that large doses are very uncertain in their action, it being exceptional for a single large dose of tartar emetic to cause the death of an adult, owing to the prompt emesis which follows. However, if a second dose follow after the symptoms resultant on the first dose have subsided, the action is more severe and often fatal. Practically all the homicidal cases on record extended over several days, death being due to administration of repeated doses. In those cases in which vomiting does not follow the taking of the antimonial, the danger of a fatal outcome from a single dose is, probably, much greater.

The smallest dose of tartar emetic that has proven fatal to a child is ¾ grain (48.5 mg.) given in an enema[7], while, in the case of an adult, it is 2 grains.[1] In a case reported by Beau[2] a woman took 1½ grains without effect and followed this, 24 hours later, with a similar dose, which caused violent vomiting and purging with death in 36 hours. However, vastly larger doses have been recovered from, as the case cited by Taylor[3] of recovery following the taking of 240 grains, the patient vomiting only once after the dose; and the case of Carpenter[4] of recovery after a dose of 170 grains.

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[1] Ann. d'Hyg., 1846, **36**, 221.

[2] *Précis de Toxicologie,* 2 ème ed., 1889, p. 189.

[3] *Traité de Toxicologie,* 5 ème ed., 1852, **1**, 618.

[4] Ann. d'Hyg., 1846, **36**, 221.

[5] Brit. Med. Jour., 1903, **1**, 873.

[6] *Studies from Lab. of Sheffield Sc. Sch.*, 1887, **2**, 68.

[7] Charier, Jour. de chim. méd., 1847, 3 s., **3**, 472. See, also, Chabon, Union méd. de la Seine inf., 1881, **20**, 114.

It is probable that the actual amount of tartar emetic which will invariably prove fatal is uncertain. As Taylor[5] remarks: "Taking the facts hitherto collected, it appears probable that under circumstances favorable to its noxious operation on the system (indicated by failure of pulsation and collapse), a dose of from *ten* to *twenty grains*, taken at once, might destroy an adult, and if taken in divided doses, a smaller quantity than this might suffice."

Fatal Period.—The most rapidly fatal poisoning with tartar emetic appears to be the case of the child, reported by Charier[6], who died within 1 hour after a dose of 3.4 grains; while with an adult cases of death in six[7] and seven[8] hours have been reported. According to Witthaus[9], "The average of 8 cases in children less than ten years of age, in which the duration is definitely stated, was 15.9 hours, the extremes being 1 and 48. In adults the average of 18 cases was 88.9 hours, or, if 5 exceptionally protracted cases are omitted, 37.4 hours, with 6 and 96 as the extremes."

Treatment.—Although vomiting is usually copious after intake of the antimonials, it is wise to wash out the stomach with warm water containing tannic acid, or large amounts of a decoction of green tea, with the object of rendering the antimony present insoluble by the formation of the insoluble tannate. This washing out of the stomach should be repeated to take care of the antimony reexcreted into the stomach. Demulcent fluids may then be given in the form of milk, egg albumin whipped up with water, or magnesium oxide. For the pain, morphine may be necessary. The cardiac and general depression are to be combated by such stimulants as strychnine, caffeine and camphor.

Postmortem Appearances.—The findings at autopsy resemble those found in arsenic poisoning. It is usual to find evidences of marked irritation of the mouth and esophagus; pustules, apthae and ulcers may be found here, as also in the stomach, although the stomach may, as is the case with arsenic, appear almost normal. Ordinarily, however, there will be found in the gastrointestinal tract some redness, swelling and ecchymotic patches, while ulceration is not so common.

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[1] Taylor, Guy's Hosp. Rep., 1857, 3 s., **3**, 369.

[2] Bull. gén. de Thérap., 1856, **51**, 231.

[3] *On Poisons*, 3rd Amer. Ed., 1875, p. 443.

[4] New York Med. Record, 1883, **24**, 401.

[5] *Loc. cit.*, p. 448.

[6] Jour. de chim. med., 1847, 3 s., **3**, 472.

[7] Ranke, Friedreich's Bl. f. ger. Med., 1879, **30**, 241.

[8] Durand-Fardel, Bull. gen. de therap., 1843, **25**, 370.

[9] *Toxicology*, 1911, p. 360.

In the chronic cases especially, and to some extent, also, in the more acute cases, fatty degeneration of the liver, kidneys and heart is more or less constant, while the lungs may show evidences of inflammation and hepatization. In the subacute and chronic cases, changes in the central nervous system may be observed, such as degeneration of the ganglion cells, and degenerative changes may be noted in the peripheral nerves. Congestion of the cerebral vessels is not infrequently found, accompanied with effusions into the arachnoid and ventricles.

Detection.—As the symptoms and postmortem findings of antimony poisoning are, in many respects, similar to those of arsenic poisoning, it remains for the chemical examinations of the tissues and excretions to differentiate between them. In this latter case, also, we find that arsenic and antimony produce somewhat similar reactions, but, fortunately, ones that may be accurately identified as related to the presence of one or the other, or possibly both, of these poisons.

Preliminary Test.—As is the case with arsenic, we have, in the *Reinsch Test*, a procedure, which permits of a definite statement as to the presence or absence of these metals. The details of this test have already been discussed on pages 466 and 507, so that we refer thereto for the methods involved. As stated previously, this test is positive only when the deposit on the copper foil has been sublimed and the sublimate identified. In the case of antimony, the sublimate is, almost always, amorphous, but as stated by Wormley[1], the antimonial sublimate *may* contain octahedral crystals, at least when a comparatively large deposit is heated, but the antimony deposit requires a much higher temperature than arsenic for its vaporization, and, being less volatile, the sublimate is very near or only slightly in advance of the copper slip, while arsenic is found higher up in the subliming tube. This test has the advantage that it can be made on the undecomposed tissues and is, therefore, of great value as a preliminary test. Should no deposit show on the copper foil, no antimony is present; and, further, should no amorphous sublimate be yielded by a stained slip of heated copper, antimony may be regarded as absent from the tissues examined. If the deposit of antimony trioxide on the subliming tube be dissolved in weak tartaric acid and this solution further acidified with hydrochloric acid, an orange-red precipitate of antimony trisulphide will form on passing hydrogen sulphide through the solution.

Determination.—Having proven that antimony is present in the tissues, urine, stomach contents, feces, etc., by the Reinsch Test, a quantitative determination may be made only after destruction of the organic matter by the method of Fresenius and von Babo or by Gautier's method, or some modification of these.

The best method of affecting this decomposition is, in the writer's opinion, that of Fresenius and von Babo, as discussed on pages 339 and 510. Antimony will be found along with arsenic, if this latter metal be present, in the precipitate produced by hydrogen sulphide in the filtrate from the decomposition of the organic matter by hydrochloric acid and potassium chlorate. This precipitate is treated as discussed on page 511 and the antimony obtained in the form of the pyroantimonate as thereon discussed, along with any tin that may be present and, possibly, traces of copper. This insoluble residue of antimony pyroantimonate[1] is boiled with a solution of tartaric acid, further acidulated with hydrochloric acid, filtered, and the solution saturated with hydrogen sulphide, when the orange-red antimony sulphide is precipitated. Filter on a Gooch filter, wash thoroughly, and dry in the oven at 100°C. As this precipitate always contains free sulphur and some moisture which is difficultly expelled, heat the residue in a current of dry carbon dioxide, when the orange-red sulphide is converted into black crystalline antimonous sulphide. If the weight of this black sulphide be multiplied by 0.7142 the result is the amount of antimony, as such, in the quantity of tissue used.

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[1] *Micro-Chemistry of Poisons*, 2nd ed., 1885, p. 275.

Instead of using the above method of determining the amount of antimony, one may employ the modified Gutzeit method as follows. Prepare the solution as directed for arsenic on page 517. Place this in the apparatus described in connection with the arsenic test and make determinations as outlined there[2].

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[1] The amount of tin and copper present is not usually of consequence in cases of poisoning by antimony, so that they may be disregarded. If they are to be separated, see *Qualitative Chemical Analysis*, by Fresenius, 17th English Ed., 1921, p. 620.

[2] See Sanger and Riegel, Proc. Amer. Acad. Arts and Sci., 1909, **45**, 21. The standard antimony solution is prepared by dissolving 2.306 grams of pure, recrystallized tartar emetic in a liter of water. This solution contains 1 mg. of antimonous oxide per cc. From this solution, others containing 0.1, 0.01 and 0.001 mg. may be prepared as required. Prepare the standard stained slips of paper just as for the test. To develop the antimony band on the sensitized paper, let the treated slips stand in a test-tube covered with normal ammonium hydroxide for 5 minutes, when a black band slowly develops.

CHAPTER XX

GASEOUS POISONS

Gases differ fundamentally from solids and liquids in their physical properties and behavior and vary widely in their mode of action in the system. The ordinary atmospheric air, as breathed, contains about 21 per cent. of oxygen, which is absolutely essential for life. The inhalation of other gases is followed by suffocation, which will be more or less rapid depending upon the amount breathed and the degree of concentration of the gas, as well as upon the deficiency of oxygen in the inspired mixture. Some gases, like nitrogen and hydrogen, replace the oxygen in the lungs and exclude its entrance into the blood, thus leading directly to a state of anoxemia; others, such as carbon monoxide, destroy the oxygen-carrying power of the hemoglobin and thus lead to death; while others exert a more or less specific action on certain organs. It is undoubtedly true that the individual in the ordinary walks of life is being constantly exposed to atmospheres which are becoming increasingly toxic, while the industrial worker is subject to hazards which are, in many cases, extremely great. Probably the number of fatalities from various types of gas poisoning is increasing yearly, even though modern sanitation is making rapid advances. "Only a few of the many industries in which chemical processes have an important rôle have succeeded in reducing the hazards from poisonous gases to a minimum."[1] The intangibility of toxic gases is such that the ordinary individual gives little thought to them and there seems to be more or less mystery associated with deaths caused by them. In commenting upon this fact Henderson and Haggard[2] say, "The reactions between a living man and the atmosphere about him are so immediate, so continual and so much a matter of course, that the normal individual passes days or even years without a thought of breathing. Several times each day he thinks of food, and not infrequently of digestion. He is interested in the principles of alimentation; he gladly accepts scientific knowledge and takes elaborate precautions in food and drink. But of respiration and the gaseous substances which he takes into his body thru the lungs he is generally oblivious. On such matters even educated and thoughtful people are now usually uninformed. And yet the way that most people die is by cessation of respiration."

There are a very large number of gases which are poisonous and which have caused death or, at least, very serious effects, but we shall limit our discussion to those of more general importance. No attempt will be made to take up the broad general principles upon which the action of gases depends, to discuss the questions of relative solubility of the various gases in the blood, or to detail the chemical and physical factors upon which their absorption and elimination may depend, referring for such points to the admirable presentation by Henderson and Haggard.[1]

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[1] See Flury, Deutsche Ztschr. f. d. ges. gerichtl. Med., 1926, **7,** 149.

[2] *Noxious Gases,* 1927, p. 15.

CARBON DIOXIDE

Carbon dioxide (CO_2), also known as carbonic acid, carbonic anhydride, fixed air, and "choke damp", is probably the most wide-spread of the toxic gases, although it does not produce serious effects except under certain conditions. It is formed in the combustion of coal and wood, in lime-burning, in explosions in mines, in blasting, in the firing of explosives, in the decomposition of organic matter, in processes of fermentation, in various chemical processes, and in the metabolic processes of the animal economy.

This gas is colorless, odorless and heavier than air, its specific gravity being 1.52 (compared with air as 1). One liter of the gas at 0°C. and 760 mm. pressure weighs 1.965 grams. On account of its relative weight, CO_2 tends to collect in low places, such as caves, old wells, pits, brewer's vats, holds of ships, silos[2] and mines. This gas finds its way from these various sources into the air which we breathe, and a large amount is given off to the air in each individual expiration. Thus, ordinary inspired air contains about 0.04 per cent. of CO_2, while expired air contains about 4 per cent. of this gas. It may be seen, therefore, that the air of enclosed spaces may become greatly vitiated, if free ventilation is not supplied to make up the deficiency of oxygen, as man under ordinary circumstances takes in about 350 cc. of oxygen and gives off 300 cc. of carbon dioxide per kilo per hour. It is probable, however, that the excess of carbon dioxide is not the only deleterious element in poorly ventilated areas. If the temperature and humidity of the living rooms are properly controlled, excess of carbon dioxide may produce little or no discomfort.[3] Further, the gradual diminution of the oxygen of the air and, consequently, of the blood and tissues plays a large role in the production of the symptoms. As has been shown, when the oxygen of the inspired air is diminished to 12 to 16 per cent. the first signs of anoxemia develop in the form of increased respiration and acceleration of the pulse; when the oxygen content is diminished to 9 to 14 per cent., the higher centers of the brain are affected, consciousness continuing but judgment becoming faulty; if the oxygen is diminished to values between 6 and 10 per cent., nausea and vomiting may appear, the subject loses the ability to perform any vigorous muscular movements, and bewilderment and loss of consciousness follow; while a reduction below 6 per cent. of oxygen produces a gasping respiration, convulsive movements, cessation of breathing, and death.[1]

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[1] *Loc. cit.*

[2] See Hayhurst and Scott, Bull. Ohio State Board of Health, 1914, **4**, 1407, for report of death of 4 men engaged in tramping silage 6 feet from top of silo.

[3] See Winslow, Amer. Jour. Pub. Health, 1917, **7**, 827; and Crowder, Ibid., 1917, **8**, 6.

Although carbon dioxide under certain conditions of concentration and time of exposure is a distinctly toxic gas, yet under ordinary circumstances that produced in the human body and excreted through the lungs acts as a definite regulator of breathing and insures a definite supply of oxygen to the system. "In fact the adjustment is so precise that the slightest increase or decrease of carbon dioxide production in the body induces immediately an almost proportional increase or decrease of the volume of breathing." The carbon dioxide, through stimulation of the respiratory center, increases respiration which furnishes the oxygen necessary to make up a possible deficit. If a proper amount of oxygen is not furnished in the inspired air, the excessive breathing may deplete the body of its carbon dioxide and a condition of acapnia supervene upon the anoxemia. When, however, the partial pressure of the carbon dioxide in the inspired air is greater than that in the lungs, the CO_2 physiologically formed is not excreted and accumulates in the system and asphyxia results. Besides the function of regulating the intake of oxygen, carbon dioxide plays a large role in maintaining the acid-base equilibrium of the system, the blood holding a considerable reserve in the form of bicarbonates, which act as "buffer" salts.

Symptoms.—The symptoms of poisoning with carbon dioxide vary with the concentration of the gas. Inhalation of the pure gas or one of very high concentration is followed by almost immediate spasm of the glottis, loss of consciousness, loss of muscular power to such an extent that the subject falls as if struck by lightning, and death from asphyxia. Such accidents have been noted when individuals have been lowered into a well or other place where the gas has accumulated. If the amount be somewhat smaller, the above symptoms will be less intense, so that the individual may be able to get out of the dangerous place before the loss of muscular power is more or less complete. Premonitory symptoms of danger are giddiness, roaring in the ears, flushing of the face, a sensation of tightness across the chest, dyspnea, rise of blood pressure, followed by drowsiness, loss of consciousness and muscular power. Convulsions may or may not occur. Usually the face is livid, but, occasionally, it may be pale.

With small amounts of carbon dioxide, the brain and spinal cord are stimulated, the blood pressure rises slightly, and there is increase in the respiration to overcome the anoxemia. In concentrations of the gas of about 0.5 per cent. most persons complain of weakness and headache, although one may become gradually accustomed to the gas and breathe an atmosphere that is much more vitiated without showing any symptoms. With concentrations of 3 or 4 per cent. there is rapid breathing

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[1] See Henderson and Haggard, *Noxious Gases*, 1927, p. 98.

(hyperpnea) and some discomfort, while a concentration of 8½ per cent. produces much dyspnea, considerable rise in blood pressure and general symptoms which become serious if the exposure continues for 20 minutes. When the concentration reaches 25 to 30 per cent., the depressant symptoms become marked, diminished respiration, fall in blood pressure, muscular weakness, coma and death intervening unless the subject is quickly removed to the fresh air.

Treatment.—The most effective treatment is prompt removal of the victim from the contaminated air and immediate inhalation of oxygen. Artificial respiration should be promptly resorted to, in order to remove the carbon dioxide as quickly as possible. General stimulants are of value, but may prove ineffective if the respiration is not soon restored, although some cases are resuscitated after long insensibility. After recovery the patient may complain of marked headache or general soreness of the body, while occasionally facial paralysis may ensue.

Postmortem Appearances.—There is, as a rule, more or less cyanosis, the face being livid and swollen, although some cases are seen in which the face is pale and placid. There is nothing especially characteristic beyond the dark color and fluidity of the blood, due to the excessive amount of CO_2. The general signs are those of asphyxia, especially characterized by the filling of the venous system and the right heart with the dark blood and congestion of the viscera including the brain.

Detection.—The analysis that is usually required in case of carbon dioxide poisoning is the determination of the amount of this gas in the air of the room or space in which the body was found. As a preliminary test of the dangerous character of the air, advantage may be taken of the fact that a lighted candle is dimmed by a diminution of the amount of oxygen and an increase of carbon dioxide in the air, or, if the concentrations of these gases be sufficiently low or high respectively, the candle flame is extinguished. Thus, this happens when the oxygen content falls to 15 or 16 per cent (114 mm. partial pressure) or when the concentration of carbon dioxide reaches 12 to 15 per cent.

As a quantitative method one may use the following procedure: Fill a 5 or 6 liter bottle with the suspected air, either by displacement or by the use of a bellows. Into this bottle pour 50 cc. of standardized barium hydroxide solution, stopper the bottle tightly and shake well for 10 or 15 minutes. By back titration with standardized oxalic acid solution, the amount of the barium hydroxide converted to the insoluble barium carbonate may be determined and from this the amount of CO_2 in the air calculated.

Instead of using the above method, one may draw a measured volume of the suspected air through an apparatus consisting of a calcium chloride tube, to remove the moisture in the air, and a weighed Geissler bulb containing sodium hydroxide solution, when the increase in weight of the latter vessel will yield the amount of CO_2 in the volume of air analyzed.

CARBON MONOXIDE

Carbon monoxide (CO), carbonous oxide, is a product of incomplete oxidation of carbonaceous matter. While it is found only rarely in nature, being formed in considerable amounts during severe lightning storms[1] and being evolved from growing kelp[2], it is, nevertheless, present to a more or less extent wherever man lives and works. This toxic gas arises from lime-kilns, brick-kilns, charcoal-kilns, from conflagrations in buildings where there is not a free supply of air, from charcoal, coke, coal, and blast furnaces[3], from ordinary stoves, grates[4], braziers and salamanders, and is found in the gases (after damp) from coal dust explosions in mines[5], in the gases from explosion of high explosives, in coal and water gas used for heating and illuminating purposes, in tobacco smoke[6] and in the exhaust gas from internal combustion engines, especially automobiles.[7] Although natural gas contains little or no carbon monoxide, yet considerable is produced from it when it is used in water heaters and in improperly arranged open fires in grates.[8] Further, this gas may be found as an impurity in ethylene used for anesthesia and fatal results follow from its use for such purposes.[9]

The amount of carbon monoxide found in the various gases mentioned above varies under different conditions. As an approximation to these values I quote a table given by Sayers and Yant.[10]

Type and Source	*Carbon Monoxide by volume per cent*
Mine explosion, immediately after dust explosion (experimental)	8.0
Mine explosion, 1 day after explosion in coal mine	1.0
Mine fire	1.0
Blasting with 40 per cent gelatin dynamite, 7 minutes after shooting 100 sticks	1.2

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[1] W. M., Science, 1920, n.s. **51,** 437.

[2] Langden, Jour. Amer. Chem. Soc., 1917, **39,** 149.

[3] See Watkins, Technical Paper 156, Bureau of Mines, 1917.

[4] See Hunter, Brit. Med. Jour., 1926, **1,** 653.

[5] See Burrell and Seibert, Miners' Circular 14, Bureau of Mines, 1916; Weissberger Wien, klin. Wchusehr, 1927, **40,** 1605.

[6] See Thompson, Lancet, 1904, **1,** 395; Fleig, C. R. Acad. d. Sc., 1908, **146,** 1776; Jones, Yant, and Berger, Reports of Investigations, Serial 2539, Bureau of Mines, 1923; Baumberger, Jour. Pharm. & Exp. Therap., 1923, **21,** 23.

[7] See Burrell and Gauger, Technical Paper 216, Bureau of Mines, 1919; Henderson and Haggard, Jour. Amer. Med. Assoc., 1923, **81,** 385; Emerson, Ibid., 1924, **82,** 227; Sayers, Reports of Investigations, Serial No. 2593, Bureau of Mines, 1924; Wilson, Gates, Owen, and Dawson, Jour. Amer. Med. Assoc., 1926, **87,** 319; McNally, Arch. Path. and Lab. Med., 1928, **5,** 43; Bloomfield and Isbell, Pub. Health Rep., 1928, **43,** 750.

[8] See Hayhurst, Amer. Jour. Pub. Health, 1923, **13,** 462; Jones and Yant, Reports of Investigations, Serial No. 2572, Bureau of Mines, 1924.

[9] See Sherman, Swindler and McEllroy, Jour. Amer. Med. Assoc., 1926, **86,** 1765; Reports of Chemical Laboratory of A. M. A., Ibid., 1927, **88,** 322; Sherman, Swindler and McEllroy, Ibid., 1228.

[10] Reports of Investigations, Serial No. 2476, Bureau of Mines, 1923.

Type and Source	*Carbon Monoxide by volume per cent*
Blasting—products of combustion of black blasting powder	10.8
Products of combustion of 40 per cent nitroglycerin dynamite	28.0
Products of combustion of 40 per cent ammonia dynamite	5.0
TNT	60.0
Blast-furnace stack gas	28.0
Bessemer furnace gas	25.0
Crucible furnace, gas fuel melting Al-Cu-Sn alloy	5.5
Arc furnace melting aluminum	32.2
Cupola gas	17.0
Coke-oven gas	6.0
Coal gas	16.0
Carburetted water-gas	30.0
Blau gas	40.0
Producer gas from coke	25.0
Producer gas from oil	5.0
Distillation coal-oil mixtures	7.4
Fuel gas	30.0
Gas range burning natural gas	0.2
Room heater burning natural gas	0.5
Automobile exhaust gas (Average of tests on 101 cars of all types)	7.0
City fire (black smoke from burning building)	0.1
Insulation burning in electric arc	0.5
Furnace gas of small house-heating hot-water system	1.0
Railroad locomotive stack gas	2.0

Carbon monoxide in the pure state is produced by heating formic or oxalic acid with sulphuric acid and, under certain conditions, by the heating of potassium ferrocyanide and sulphuric acid. It is generated, also, in such industrial processes as the manufacture of acetone, rosolic acid and the Leblanc method of producing soda. It is a colorless and tasteless gas, with practically no odor except when in the pure state, when it may have a slight garlic-like odor. However, this odor is not usually noticed, so that the gas is especially dangerous on account of its freedom from odor. It is only very slightly soluble in water, its solubility at 40°C. being only 0.0178 per cent. by volume. Its specific gravity is 0.967 as compared with air, one liter weighing 1.25 grams at 0°C. and 760 mm. pressure. It burns in air with a blue flame and forms explosive mixtures with ½ of its volume of oxygen or with 2½ volumes of air. It combines with such metals as nickel and iron to form colorless liquids known as carbonyl, from which heat liberates the gas and deposits the metal. With chlorine it combines to form carbonyl chloride (phosgene), which is a poisonous gas and was used as such during the World War.

Poisoning with pure carbon monoxide is rare except in laboratories, Sachs[1] referring to the poisoning of the chemists Wharmby and Cheneau by it. Owing to the presence of carbon monoxide in the various gases above-mentioned, it is possible that fatal poisoning may arise from any of these sources, especially if the exposure be prolonged, and the literature reveals not infrequent instances of such poisonings. The most frequent source of this type of poisoning, however, is illuminating gas, which contains variable amounts of CO, ranging from 4 to as high as 16 per cent. in coal gas and from 30 to 40 per cent. in water gas. In New York City in 1925 there were reported 388 suicides, 3 homicides, and 618 accidental deaths from this cause; while in 1926 the figures were 371 suicides, 7 homicides, and 812 accidental deaths.[1] From 1905 to 1921 inclusive the Coroner's office of Cook County, Illinois reported 2509 suicides, 126 homicides, 2264 accidental deaths, and 1132 undetermined cases.[2] The figures in other cities are proportionately as large. There is a certain factor of safety in the odor of the illuminating gas. This odor, however, is not usually perceived by persons asleep or with defective sense of smell, so that sufficient gas may escape into a room to prove fatal before the victim realizes the fact. Further, the removal of the odorous constituents from illuminating gas in "scrubbing" the gas may result in poisoning through the absence of the warning odor. A leaky gas main may be the source of the toxic gas, which may lose its odor by filtration through the ground and find its way into apartments some distance from the leak, in which case it may be difficult to trace the source of the poisoning.

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[1] *Kohlenoxyd-Vergiftung*, 1900, p. 14.

Many deaths have been reported, especially in France and other continental countries, from the gas escaping from charcoal braziers and from bath-room heaters. In our country such cases are rare, although they do occur. In this connection it must be mentioned that fatalities have occurred from natural gas heaters, the CO being liberated by the excessive gas flow from too large orifices and by the relatively small air supply furnished to the heater.[3]

The number of deaths reported in America from poisoning by automobile exhausts is rapidly increasing, in spite of the frequent warnings sent out by the various health authorities throughout the country. The amount of CO in such gas ranges from 1 to 7 per cent or higher, so that the air in the region of a running auto may soon become vitiated.[4] It has been estimated that the content of CO may rise to about 100 parts per million of air in streets where traffic is congested,[5] while in Chicago streets[6] 85 per cent. of 649 samples showed 50 parts per million

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[1] Report of the Chief Medical Examiner of the City of New York, 1925 and 1926.

[2] See "Gaseous Poisons" by Doremus and McNally, in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 300.

[3] See Jones and Yant, Reports of Investigations, Serial No. 2572, Bureau of Mines, 1924.

[4] It has been shown that the use of ethyl-gasoline does not affect materially the percentage of CO contained in the exhaust gases. See, Yant and Berger, Reports of Investigations, Serial No. 2908, 1929.

[5] See Bloomfield and Isbell, Pub. Health Rep., 1928, **43**, 750.

[6] Connolly, Martinek and Aeberly, Amer. Jour. Pub. Health, 1928, **18**, 1375; Martinek and Marti, Ibid., 1929, **19**, 293.

(0.5 parts or less per 10,000). If such air be confined while the auto is running, the air in the garage soon becomes highly toxic. "A rough estimate of the volume of carbon monoxide that an automobile may produce is one cubic foot (28 liters) per minute per 20 horse power. This is sufficient to render the atmosphere of a single car garage deadly within 5 minutes, if the engine is run while the garage doors are closed."[1] In this connection Mätje[2] calls attention to the fact that a machine standing still pours forth in the exhaust gas 6 or 7 times as much CO as when the car is running on the road with a load. It is difficult to give statistics on the number of fatalities from this cause, but it is certain that a case occurs every few days in our large cities, especially in cold weather, McNally, for instance, recording 63 deaths from CO poisoning in private garages in Chicago during the last 6 years.[3]

Action.—Carbon monoxide does not irritate the air passages, so that it may be freely respired. This gas has, however, a very marked affinity for the hemoglobin of the blood, displacing, molecule for molecule, the oxygen which is combined in the form of oxyhemoglobin, thus preventing the normal oxygen-carrying power of the blood[4] and causing the tissues to suffer for want of oxygen (anoxemia). This action of carbon monoxide is regarded as the important one in the toxicology of this gas. The CO-hemoglobin is split into its constituents of CO and hemoglobin when exposed to light, while oxyhemoglobin is quite stable to light. There appears to be some evidence that CO has some toxic effects other than that above mentioned. Haldane[5] has shown that cockroaches will live for long periods in a mixture of 80 per cent. CO and 20 per cent. O_2 and that mammals can live on oxygen dissolved in their blood under high pressure even when almost all of their hemoglobin is combined with CO. Warburg[6] found, however, that when the proportion of CO to O_2 was raised to about 5, the oxygen consumption of yeasts and bacteria was diminished. Macht[7] observed that solutions of carboxy-hemoglobin inhibited the growth of seedlings of *Lupinus albus*, while Haldane[8] showed that the movements of the moth and the germination of cress seed are inhibited by CO, the greater the partial pressure of oxygen, the more carbon monoxide being required. This latter worker found, further, that rats living on oxygen dissolved in their blood in presence of sufficient carbon monoxide to combine with almost all their hemoglobin are killed by the addition of more CO, so that he reached the conclusion that CO is a tissue poison destroying a catalyst of oxidation resident in the tissue cells.

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[1] See *Noxious Gases* by Henderson and Haggard, 1927, p. 105.

[2] Zentralbl. f. Gewerbehyg., 1927, **14**, 275.

[3] Arch. Path. and Lab. Med., 1928, **5**, 43.

[4] In this connection see the work of Warburg on "The Chemical Constitution of Respiratory Ferment", Science, 1928, **68**, 437.

[5] Jour. Physiol., 1895, **18**, 201.

[6] Biochem. Ztschr., 1926, **177**, 471.

[7] Science, 1927, **66**, 198.

[8] Biochem. Jour., 1927, **21**, 1068.

The displacement of oxygen by carbon monoxide is a reversible action, the carbon monoxide being, also, displaced by oxygen, although the union of hemoglobin with carbon monoxide is a much more stable one than the combination with oxygen. The tensions of the two gases which will exert an equal combining power vary greatly, that of carbon monoxide being approximately 300 times that of oxygen according to Sayers and Yant[1] and Henderson and Haggard[2], while Nicloux[3] gives this relationship as 220 to 1 and Anson, Barcroft, Mirsky and Oinuma[4] state that this value is about 250 to 1 at 37° C. and 400 to 1 at 15° C. The relative amounts of these two gases in the air will determine the proportion in which the combination with hemoglobin will take place, but it must be remembered that the amount of absorption of the bases is limited by the volume of respiration, so that the theoretical percentage combination will not be reached for many hours of exposure to low concentrations of carbon monoxide. The chemical reaction of carbon monoxide poisoning is that of a reversible mass action, the tendency being to establish equilibrium between carbon monoxide hemoglobin and oxyhemoglobin, and can be made to proceed in either direction by changing the mass or tension of the gases in the pulmonary air. Further, complete equilibrium will probably not be established, as the tendency of the carbon monoxide hemoglobin is to dissociate into carbon monoxide and hemoglobin as the amount of the carbon monoxide hemoglobin increases, so that the reaction is slowed down appreciably as the point of saturation is reached. "As the reaction approaches equilibrium, the balance of pressure between the oxygen and carbon monoxide in the blood, and of their attraction for hemoglobin shifts automatically and progressively until at equilibrium carbon monoxide is displaced by oxygen in amount each minute equal to that in which oxygen is displaced by carbon monoxide."

As the amount of absorption of carbon monoxide is, as stated above, proportional to the volume of inspired air, it follows that the time required for saturation of the hemoglobin with carbon monoxide will decrease as the concentration of the gas rises, so that a concentration of 0.1 per cent. for instance, would require several hours exposure before a fatal saturation was reached, while a concentration of 1 per cent. would prove fatal in a few minutes. Further, the state of activity of the subject has a great influence on the amount of possible absorption of the toxic gas. Thus, a person doing moderate exercise breathes approximately twice as much air as one at rest and will, therefore, absorb CO about twice as fast, while an individual doing heavy work may breathe three or four times as much as one at rest and will, as a result, absorb correspondingly more carbon monoxide. Also, if the respired air contains a diminishing amount of oxygen, the amount of oxygen in the pulmonary air will decrease and the lung ventilation will increase, both of which factors increase the amount of CO which will be in combination with hemoglobin for a given percentage of CO in the air. A further influence on the absorption of CO is furnished by high temperature and high humidity, both of which cause increased respiration and increase the rate of absorption of CO by the blood.[1]

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[1] Reports of Investigations, Serial No. 2476, Bureau of Mines, 1923.

[2] *Noxious Gases*, 1927, p. 106.

[3] Presse méd., 1917, **25**, 153; Ibid., 1921, **29**, 701.

[4] Proc. Roy. Soc. London, B., 1924, **97**, 61.

As Henderson and Haggard state, "When two individuals, one of whom is much larger than the other, or when an adult and a child, both at rest, are exposed to the same atmosphere, it is the smaller and younger individual with the more active metabolism, who absorbs carbon monoxide and tends to approach saturation the more rapidly. In such cases it is the relation of the volume of respiration to the size of the body and its volume which influences the rate at which oxygen is displaced by carbon monoxide. In the resting state the volume of breathing varies between individuals as a function of the surface area of their bodies; the volume of blood on the other hand varies as the weight of the body . . . Small individuals therefore succumb to carbon monoxide more rapidly than large individuals, for the volume of their respiration is greater in relation to their volume of blood." While there is little difference in susceptibility of the two sexes to the action of such gases as carbon monoxide, yet the female, being somewhat more accustomed to breathe the vitiated air of the house, has, possibly, a slightly greater resistance to its action[2].

While the hemoglobin of the red cell is not able to perform its normal function of carrying oxygen to the tissues, owing to the combination of carbon monoxide with it, the degree of poisoning depends upon the extent of that inability, or in other words upon the degree of saturation of hemoglobin with CO, and, also, upon the time during which the resulting anoxemia has continued. A long exposure to a low concentration of CO will, probably, produce more serious effects than will a short exposure to a high concentration, assuming that the degree of saturation of the hemoglobin with CO is the same in each case, simply because the anoxemia has continued longer in the former instance. The red cells, in which the hemoglobin has combined with carbon monoxide and then has been freed from this combination by oxygen inhalation, are not at all injured by this process, but are able to take up again their normal oxygen-carrying functions. The after-effects of the poisoning are due to secondary effects brought by the anoxemia. "During the first hour after moderate degrees of gassing, one-half, or a little more, of the gas that has been absorbed is eliminated under ordinary circumstances; complete elimination under the action of fresh air is not affected for many hours, however. After brief exposure to a high concentration of the gas with rapid absorption, the anoxemia is therefore suffered mainly during the period of elimination." Romanese[1] is of the opinion that the action of carbon monoxide is not yet fully cleared up, believing that neither the asphyctic nor the toxic theory explain all cases.

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[1] Sayers, Meriwether, and Yant, Pub. Health Rep., 1922, **37**, 1127.

[2] In this connection see the case of Pehl et al *v.* Butt et al, cited on page 85.

Symptoms.—The symptoms of carbon monoxide poisoning will depend, of course, upon the concentration of the gas and the rate of absorption. As a rule the entrance into an atmosphere of high concentration is followed by almost immediate unconsciousness, with sudden loss of muscular power and failure of respiration and cardiac activity[2]. In such cases the person may die within a very few minutes, even though the conversion of the oxyhemoglobin into carboxy-hemoglobin may be far from complete.

The most frequent cases, however, are those which result in gradual development of the symptoms from a more or less prolonged exposure to concentrations of relatively small proportions. These symptoms vary in individual cases, rarely all of them being observed in any single case. There are sensations of tightness across the forehead, severe frontal and basal headache, dilatation of the cutaneous vessels, flushed face, bright red patches on the skin, lachrymation, buzzing in the ears, throbbing in the temples, weakness, somnolence, dizziness, nausea and vomiting. The respiration is at first accelerated and irregular and, later, becomes slower and is often associated with severe dyspnea and a sensation of weight in the chest. The cardiac action is at first accelerated and later becomes slow and irregular, the blood pressure being first increased and later diminished. Forbes, Cobb and Fremont-Smith[3] have shown that there is a rise in intracranial pressure, which shows two distinct elevations, the first occurring during asphyxia and being caused by congestion, and the second occurring after asphyxia and probably caused by edema. These symptoms are related to a stimulation of the nervous system followed by a paralysis, in which loss of muscular control, especially of the sphincters, loss of reflexes, coma with intermittent convulsions, Cheyne-Stokes respiration, followed by gradual cessation of respiration and cardiac action and death are noted.

The symptoms noted will vary with the degree of saturation of the hemoglobin with carbon monoxide, the symptoms being much more severe if a given saturation has been reached by long exposure to low concentrations than when the same degree of saturation has been acquired by a short exposure to high concentrations. This fact may be noted from the following table given by Sayers and Yant[4].

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[1] Arch. di antrop. crim., 1927, **47**, 959. Abstract in Arch. Pathol., 1928, **6**, 154.

[2] See Prati, Arch. di antrop. Crim., 1927, **47**, 1007. Abs. in Arch. Pathol., 1928, **6**, 154.

[3] Arch. Neurol. & Psychiat., 1924, **11**, 264.

[4] Reports of Investigations, Serial No. 2476, Bureau of Mines, 1923.

Percentage of Blood Saturation	*Symptoms*
0–10	No symptoms.
0–20	Tightness across forehead; possibly slight headache, dilatation of cutaneous vessels.
20–30	Headache, throbbing in temples.
30–40	Severe headache, weakness, dizziness, dimness of vision, nausea and vomiting, collapse.
40–50	Same as previous item with more possibility of collapse and syncope, increased respiration and pulse.
50–60	Syncope, increased respiration, and pulse; coma with intermittent convulsions; Cheyne-Stokes respiration.
60–70	Coma with intermittent convulsions, depressed heart action and respiration, possibly death.
70–80	Weak pulse and slowed respiration; respiratory failure and death.

The recovery from the effects of carbon monoxide poisoning is, in some cases rapid, while in others it is a slow process. There is probably no doubt that some persons build up a specific tolerance to the deprivation of oxygen, so that they experience little or no effect from a concentration which may be serious with others. The after-effects may be headaches, muscular pains, loss of strength, loss of memory, multiple neuritis, paralysis and temporary blindness, all of which usually clear up in a few days, but occasionally have lasted for many weeks.[1]

Chronic Poisoning.—This type of poisoning arises from the daily, more or less constant or repeated absorption of small quantities of carbon monoxide from whatever source it may arise. Workers in industrial plants are not infrequently exposed to absorption of this gas arising from blast furnaces, while those employed about gas works are exposed to a greater hazard. In the home the sources of CO are many and are ordinarily disregarded by most individuals. Many of us are constantly subjected to the possibility of absorbing carbon monoxide, which may arise from leaky gas fittings, incomplete combustion of carbonaceous matter in stoves, grates, and furnaces, loose stove-pipe joints, defective "breeching" connecting furnace and flue, down-drafts forcing products of incomplete combustion from the furnace into the furnace room, leaky rubber tubing used to connect gas heaters, etc. Other sources of possible inhalation of this gas arise from the constantly increasing contamination of the air of our city streets with automobile exhaust, from defective heaters in autos, from inhalation of tobacco smoke in places where many are smoking, etc. It is probably true that few persons realize the possibility of danger from these gases and pay little attention to the premonitory symptoms which may be present. Further, it is rare for the practicing physician to recognize the condition of chronic poisoning and to attribute the varied complaints of his patients to the proper cause.

While the absorption of small amounts of carbon monoxide for a short time may produce no symptoms, a saturation of 10 to 20 per cent.

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[1] See "Multiple Neuritis Following Carbon Monoxide Poisoning" by Wilson and Winkleman, Jour. Amer. Med. Assoc., 1924, **82,** 1408.

of the hemoglobin with CO having been shown to be without effect, yet when the time of exposure is prolonged the amount of absorption increases and the degree of saturation may increase to the point of causing distinct symptoms of poisoning. In acute cases of carbon monoxide poisoning the normal elimination requires several hours, usually 8 to 15, to reduce the carbon monoxide to the point of 10 per cent. saturation of the total hemoglobin. In chronic cases, however, the initial saturation is low, it is true, but there is, for some hours after the exposure, a retention of an undeterminate amount of CO. If, therefore, the inhalation of the carbon monoxide continues or is repeated, there is an additive or cumulative effect of the CO, which will continue just as long as the inhalation keeps up. This cumulative effect is a function of the time of exposure and the concentration of the gas. If we express the time in hours and the concentration in parts per 10,000, according to Henderson and Haggard[1], we have the following:

Time × Concentration = 3, no perceptible effect.
Time × Concentration = 6, a just appreciable effect.
Time × Concentration = 9, headache and nausea.
Time × Concentration = 15, dangerous.

While there may be some elimination of the absorbed CO during the time in which the person is not actively exposed to the gas, yet it must be remembered that the affinity of hemoglobin for CO is 300 times greater than for O_2 and, as a result, the intake of oxygen will not be sufficient to remove all the combined CO. It is clear, therefore, that, when the exposure to CO is constant or repeated, sooner or later the blood saturation will reach the point at which definite symptoms will be manifest, although CO may be detected in the blood long before such a degree of combination with hemoglobin has been reached. In a series of experiments by Sayers, Meriwether and Yant[2], it was found that persons exposed to concentrations of 2 parts of CO per 10,000 (0.02 per cent. or 200 parts per million) for 6 hours showed a 16 to 20 per cent. saturation of the hemoglobin but no symptoms; with exposure to 3 parts per 10,000 for 4 hours the saturation was 22 to 24 per cent. and the symptoms where mild in character; and on exposure to 4 parts per 10,000 for 2 hours the saturation was practically the same as in the previous exposure to 3 parts per 10,000 and the subjects showed persistent yawning and slight headache in 1 hour and dizziness, intense headache and palpitation on climbing stairs after 1½ hours, the after-symptoms being headache, irritability, dulness and inability to sleep well. In investigations conducted by Sayers, Yant, Levy and Fulton[3], in which six men were exposed 4 to 7 hours daily over a period of 68 days to gasoline engine exhaust gas-air mixtures containing 2, 3, and 4 parts of CO per 10,000 of air, the following conclusions were made: Exposure to 2 parts CO per 10,000 of air caused some subjects at rest or exercising mildly to experience slight but not discomforting symptoms in approximately 2 hours and distinct frontal headaches in 3½ to 4 hours, the blood attaining 20 per cent saturation in 3½ to 4¼ hours and 25 per cent. in 5 and 6 hours, depending on the person and whether he was at rest or exercising mildly. Exposure to 3 parts CO per 10,000 of air caused some subjects to experience slight symptoms in less than 2 hours and distinct frontal headaches in 2½ to 3 hours, the blood reaching a saturation of 20 per cent. in 2½ to 3½ hours, 25 per cent. in 3 to 4 hours, and 30 per cent. in 4 to 5½ hours. Exposure to 4 parts CO per 10,000 of air caused frontal headache in 1½ to 2 hours, the blood reaching a saturation of 20 per cent. in 1¼ to 2¼ hours, 25 per cent. in 2¼ to 3¼ hours, and 30 per cent. in 3 to 4 hours. With these different concentrations, exercise, even though mild, augmented the absorption of CO and caused symptoms to appear after shorter exposure. The rate of elimination of CO from the blood in a given period after exposure varied directly with the initial saturation. After an initial saturation of 35 per cent. was attained, approximately 1½ hours was required to lower it to 30 per cent., about 1 hour more to lower it to 25 per cent., nearly 1½ hours to lower it to 20 per cent., nearly 2 hours more to lower it to 15 per cent., 2½ hours more to lower it to 10 per cent., and 3 to 5 hours longer to lower the saturation to 5 per cent., if the subject breathed air the entire time. A 30 minute inhalation of oxygen or 5 per cent. carbon dioxide in oxygen reduced the CO-hemoglobin from 35 per cent. to less than 10 per cent. in 30 minutes, and when given immediately it alleviated the symptoms. There were no apparent signs that the tests produced deleterious effects to the health and physical well-being of the subjects exposed to these concentrations for such long periods.

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[1] Jour. Ind. and Eng. Chem., 1922, **14**, 229; Jour. Amer. Med. Assoc., 1923, **81**, 385. See, also, *Noxious Gases*, 1927, p. 109, whereon these figures are given in parts per million.

[2] Reports of Investigations, Serial No. 2338, Bureau of Mines, 1922.

[3] *Effect of Repeated Daily Exposure of Several Hours to Small Amounts of Automobile Exhaust Gas*, Public Health Bulletin, No. 186, March, 1929.

Symptoms.—The symptoms of the chronic type of carbon monoxide poisoning will vary with the time of exposure and degree of concentration of the gas, just as does the acute form. No symptoms, beyond slight fatigue, will probably be noted until the blood becomes at least 20 per cent saturated. Beyond this point the symptoms increase in severity as saturation increases and include progressive fatigue, muscular weakness, headache, dullness and mental depression, disturbed vision, a peculiar transient ashy pallor which may change to a more or less greenish pallor, red patches on the cheek bones, palpitation of the heart (especially on slight exertion), nausea, vomiting, vertigo, slowing of the pulse, and dyspnea. The weakness may become marked and be associated with a great desire to sleep.[1] Luden believes that there is a close relationship between endocrine insufficiency and the effects of carbon monoxide poisoning. While long continued absorption of this gas may, in some cases, produce an anemia, yet this would seem to be evident more from the marked pallor than from the blood findings, as many workers have found that there is, in the majority of cases, a polycythemia, which may reach as high as nine million red cells per cubic millimeter.[1] Bianchini and Fabborni[2] report an increase of the platelets to twice their number, but state that there is a rather rapid return to normal shortly after the exposure to the gas has ceased.

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[1] See McCombs, Amer. Jour. Med. Sci., 1912, **144,** 577; McGurn, Interstate Med. Jour., 1917, **24,** 479; Luden, Mod. Med., 1921, **3,** 102 and 167; Egdahl, Jour. Amer. Med. Assoc., 1923, **81,** 282; Stevens, Ibid., 1926, **86,** 1201; Battley, Canad. Med. Jour., 1923, **19,** 157.

Lethal Dose.—This depends entirely on the time of exposure and the concentration of the gas. When the saturation of the hemoglobin reaches 70 to 80 per cent., death is imminent unless rapid treatment is instituted. A concentration of 1 per cent. will prove fatal in a very short time, two to five minutes exposure, while a lower concentration, such as 0.5 per cent., would not produce fatal results for 15 or 20 minutes in all probability. Much depends on the activity of the individual at the time of exposure, as absorption is more rapid in states of activity than when the person is at rest. A concentration of 0.2 per cent. would, undoubtedly, prove fatal if the exposure were continued for 1 to 2 hours. Death ensues when the saturation of the hemoglobin reaches about 70 per cent., or, in other words, when the oxyhemoglobin is reduced to about 30 per cent. of the normal. It follows, therefore, that the blood of an individual poisoned with carbon monoxide never reaches complete saturation with this gas.

Treatment.—In the treatment of carbon monoxide poisoning the most important measure is to remove the CO from the blood as rapidly as possible and thus prevent the continued anoxemia. The principal factors contributing to such a result are (1) the removal of the subject from the contaminated air as quickly as possible, (2) the restoration of respiration, if possible, in cases in which breathing has stopped, or is weak and intermittent, (3) the increase of the amount of oxygen in the inspired air, and (4) the increase in the lung ventilation. Although the patient may die of asphyxia in carbon monoxide poisoning as well as in drowning or after an electric shock, the situation is somewhat different in these cases. As Henderson and Haggard point out, "The points to be clearly understood in connection with the treatment of asphyxia are that the essential condition consists, not in cessation of breathing, for respiration continues almost to death; but in the interruption of the supply of oxygen to the tissues of the body, and especially to the brain. In this respect asphyxia by gases contrasts with drowning and electric shock. In both of these conditions spontaneous respiration is stopped, and artificial respiration is the supremely important measure of assistance.

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[1] See Haines, Karasek and Apfelbach, Report of Illinois Commission on Occupational Diseases, 1911, p. 89; Forbes, Jour. Ind. Hyg., 1921, **3**, 13; Egdahl, Jour. Amer. Med. Assoc., 1923, **81**, 282; Beck and Fort, Ann. Clin. Med., 1924, **3**, 437.

[2] Pathologica, 1922, **14**, 230; Chem. Abs., 1923, **17**, 3366.

Inhalation of oxygen and carbon dioxide is then merely a useful accessory. After a prolonged severe asphyxia, on the contrary, the victim, unless irretrievable, is generally breathing spontaneously, altho poorly."

The first step in the treatment is to remove the subject immediately to *fresh but not cold air.* If the patient be breathing, although it may be slowly and intermittently, he is given an inhalation of oxygen containing 5 per cent of carbon dioxide. The addition of the carbon dioxide stimulates the respiratory center and increases the lung ventilation. It has been found that inhalation of pure oxygen will remove the carbon monoxide practically 4 times as fast as will normal air, while the mixture with 5 per cent. carbon dioxide in oxygen removes the CO 5 to 6 times as fast as normal air.[1] The inhalation of oxygen and carbon dioxide is continued for 15 to 30 minutes after spontaneous respiration commences. As Sayers and Yant[2] point out the use of oxygen alone, instead of the combination with carbon dioxide, has the advantage that it is more available due to its use in the industries for other purposes. Both of these inhalation treatments are given preferably with an inhaler, but apparatus may be improvised if necessary.

If the patient is not breathing, the inhalation treatment will, of course, be ineffective until some method of artificial respiration is instituted. For this purpose the manual prone pressure method of Schäfer is by far the best. The procedure to be followed is as follows: Lay the patient on his belly with his face to one side so that his nose and mouth are free for breathing. Extend one arm straight out beyond his head and bend the other at the elbow, allowing the head to rest on this bent arm. Now kneel, straddling the victim's thighs and facing his head. Place the palms of the hands on the victim's short ribs, with the thumbs parallel with the spine and about two inches apart, the fingers being spread out as much as possible (Fig. 44). With arms held straight, swing forward slowly while counting one, two, so that the weight of your body is gradually but not violently, brought to bear upon the patient (Fig. 45). This act should take about two seconds. Now, while counting three and leaving your hands in place, swing backward slowly so as to remove the pressure, and, while counting four and five, rest. Repeat these operations deliberately, swinging forward and backward twelve to fifteen times a minute, thus making a complete respiration in four or five seconds. While this artificial respiration is being continued, an assistant should draw forward the patient's tongue if it has fallen back and should hold it out if it tends to draw back. Keep bystanders from crowding around and shutting off the fresh air. As soon as artificial respiration has been started, and while it is being continued, the assistant should loosen all tight clothing about the patient's neck, chest or waist and wrap the patient warmly with a blanket. Hot bricks, bottles or rubber bags filled with hot water may be used to keep the patient warm, but care must be taken not to burn him, as very troublesome results may follow. This artificial respiration should be continued without interruption for several hours, if necessary. Do not stop the efforts at resuscitation

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[1] See Henderson and Haggard, Jour. Pharm. and Exp. Therap., 1920, **16,** 11; Henderson, Haggard and Coburn, Jour. Amer. Med. Assoc., 1920, **74,** 783; Ibid., 1921, **77,** 424; Haggard and Henderson, Ibid., 1065; Report 1 of Commission on Resuscitation from Carbon Monoxide Asphyxia to American Gas Association, Ibid., 1922, **79,** 1137; Sayers and O'Brien, Pub. Health Rep., 1922, **37,** 271; Drinker, Drinker, Shaw and Redfield, Jour. Ind. Hyg., 1923, **5,** 109; Final Report of Commission on Resuscitation from Carbon Monoxide Asphyxia, Ibid., 125; Sayers and Yant, Pub. Health Rep., 1923, **38,** 2053; Sayers, Yant and Jones, Ibid., 2311; Drinker, Jour. Indus. Hyg., 1923, **5,** 255; Panis and Salmon, Presse méd., 1924, **32,** 272; Henderson, Jour. Amer. Med. Assoc., 1924, **83,** 758; Nicloux, Nerson, Stahl and Weill, C. R. Soc. de biol., 1925, **92,** 178; Walton, Eldridge, Allen and Witherspoon, Arch. Int. Med., 1926, **37,** 398; Henderson and Haggard, Jour. Amer. Med. Assoc., 1929, **92,** 434. Report 1 of the Committee on Poisonous Gases of the American Medical Association, Jour. Amer. Med. Assoc., 1930, 94, 179; Henderson, Haggard, Coryllos and Birnbaum Arch. Int. Med., 1930, 45, 72.

[2] Reports of Investigations, Serial No. 2476, Bureau of Mines, 1923.

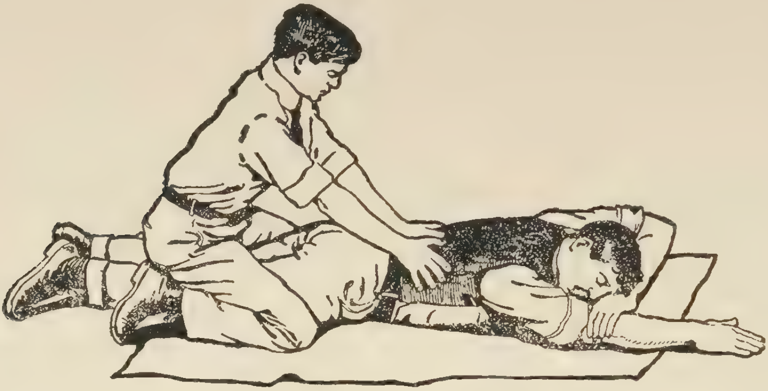

FIG. 44.—First step in Schäfer's method of artificial respiration. (Courtesy of Bureau of Mines.)

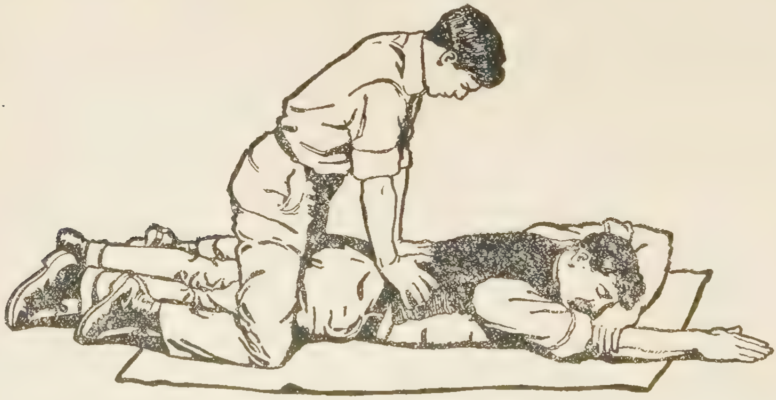

FIG. 45.—Second step in Schäfer's method of artificial respiration. (Courtesy of Bureau of Mines.)

until certain that the patient is dead and can not be revived. If the natural breathing should stop, after being once restored, repeat the artificial method again.[1]

Such mechanical devices as the pulmotor and lungmotor to resuscitate "gassed" subjects, have been advocated and frequently used, but there can be little question that they are far inferior to manual methods of artificial respiration. Not only do they require greater training and experience than does the method outlined above, but they are rarely obtainable when wanted. The time spent in waiting for their arrival would much better be spent in attempting to resuscitate the victim by manual methods. "Time is the most essential factor in resuscitation; every minute lost after breathing has stopped, and before artificial respiration is begun, decreases the chance of recovery." It is probably true that these devices have done more harm than good and have led to the loss of many more lives than they have ever saved, as Henderson and Haggard state. There is a possibility, as shown by animal experiments,[2] that acute cardiac dilatation and failure of the right ventricle may occur in "gassed" subjects as a result of excessive artificial respiration by such positive pressure apparatus. The "Drinker respirator" seems to give very satisfactory results.[3]

After natural breathing has been restored, the patient should be kept flat and should be moved only on a stretcher. It is dangerous to allow a patient, who has been overcome with carbon monoxide, to sit up or stand and an attempt to walk may cause sudden death. The period of rest should be continued for some time until the danger of cardiac failure is past. The after-treatment should be symptomatic and especially designed to prevent the development of pneumonia. Under no circumstances should any liquids be given by mouth until the patient is fully conscious. Transfusion of blood has been employed occasionally, but it has little value unless used early in the poisoning, as the elimination of the CO proceeds to such a point that transfusion soon becomes unnecessary. The intravenous injection of hypertonic saline solution may be of value in relieving the after effects of the poisoning. de Vevey[4] advocates the administration of sodium hyposulphite. The ordinary dose is from 8 to 20 grams given dissolved in water over a period of 24 hours. If the patient is in coma and is unable to swallow, the solution may be introduced into the stomach by a nasal sound or given as a lavage. In urgent cases the physician may inject intravenously 25 cc. of a 10 per cent. solution, prepared with boiling water and filtered through a sterile cloth. He advocates the continuation of the drug for a week after recovery.

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[1] See Schäfer, Harvey Society Lectures for 1907–08, New York, 1909.

[2] Drinker, Drinker, Shaw and Redfield, Jour. Ind. Hyg., 1923, **5**, 109.

[3] See Drinker and McKhann, Jour. Amer. Med. Assoc., 1929, **92**, 1658; Wightman and Shaughnessy, Ibid., 1929, **93**, 456.

[4] Paris letter, Jour. Amer. Med. Assoc., 1930, **94**, 1081.

It has been stated that firemen, who are forced to enter burning buildings, or miners working in places in which they may be exposed to carbon monoxide or other gases, should wear gas masks such as those employed by the U. S. Army. While such masks may prevent the absorption of the toxic gas, yet they do not protect the individual against a deficiency of oxygen in the air, a condition which may prevail very frequently. Gas masks are now available containing in their canisters some one or more of eight general types of material for absorbing the toxic gas,[1] the absorbent for CO being known as "hopcalite"[2], a granular mixture of specially prepared basic copper carbonate and manganese dioxide. This agent acts as a catalyst causing carbon monoxide and oxygen present in the air passing through it to unite and produce carbon dioxide. Such masks, however, afford protection for relatively short periods, such as 30 minutes[3], and can not furnish a supply of oxygen to make up for the deficiency in the inhaled air. As Fieldner, Katz and Kinney[4] have shown, firemen have been overcome while wearing Army gas masks for fighting fires, although such masks give excellent protection against smoke and the irritating products of combustion. Caution concerning the use of canister gas masks in mines can not be too strongly emphasized, as the air in mines may be depleted of its oxygen as a result of fires or explosions or by absorption of the oxygen or dilution of the air with other gases from the mine. It is advisable, rather, to employ a self-contained oxygen breathing apparatus as this affords complete protection against all gases and furnishes a supply of the vital oxygen. This apparatus is a portable device for supplying oxygen, which the wearer continually rebreathes, while the carbon dioxide exhaled is absorbed by an alkali, one type of this apparatus affording safety for about 30 minutes and a second type supporting life for 2 hours. As Henderson and Haggard remark, "The apparatus is largely used in mine rescue work and to some extent by firemen. For purposes of exploration work and rescue over considerable distances in atmospheres deficient in oxygen, where the flame of a safety lamp is extinguished, self-contained breathing apparatus is the only means available. On the other hand, for use even in very poisonous atmospheres, in which there is sufficient oxygen to support a flame, the gas mask and canister afford not only a more practical condition for the wearer to do the work for which he has come, but also a greater degree of safety; certainly with far less liability to accident."

Postmortem Appearances.—The findings at autopsy in cases of carbon monoxide poisoning are quite characteristic in most cases, although in some cases of death from relatively small amounts of the gas or occurring some hours after exposure very few changes may be found. The characteristic action of CO, when absorbed, is the formation of carboxyhemoglobin, as a result of which the blood assumes a bright cherry-red color. On this account the color of the skin and of the visible mucous membranes of the victim of carbon monoxide poisoning is more or less rose-red in tint and red spots appear on the face, neck, breast and extremities, the dependent parts of the surface of the body being of a somewhat deeper red than other parts. This rose-red color of the skin has, not infrequently, led the laity to doubt that death has taken place.[1] Occasionally these red spots may not be observed, but their absence should not be interpreted as meaning that carbon monoxide poisoning has not occurred. On the other hand, the appearance of the skin and the red spots should not be taken to mean, necessarily, that CO poisoning has occurred, as these colorations are very similar to those found on a corpse which has lain exposed to the cold or on bodies of persons poisoned with benzol or potassium cyanide. On opening the body, the blood is found to be bright cherry-red in color and the internal organs show this same red coloration both on their surfaces and on cut section. This rosy color of the viscera may last for some time, Stevenson[2] reporting a case in which the coloration was visible after 17 months. The muscles also take on this reddish tone, the CO remaining longer in them than in the blood.

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[1] See Henderson and Haggard, *Noxious Gases*, 1927, p. 197.

[2] See Lamb, Bray and Frazer, Jour. Ind. and Eng. Chem., 1920, **12**, 213.

[3] In this connection see "The Carbon Monoxide Self-Rescuer" by Fieldner, Katz and Reynolds, Reports of Investigations, Serial No. 2591, Bureau of Mines, 1924.

[4] Technical Paper 248, Bureau of Mines, 1921.

The blood is usually fluid, though not always, although Forbes and Hompe[3] have shown that the coagulating power is not changed. In some cases the blood may be clotted in the heart and aorta, and thrombosis with secondary embolism and gangrene of the extremities may occur.[4] Occasionally, degenerative changes may be found in the walls of the blood vessels.

The digestive tract may show hyperemia, ecchymoses, effusions, or extensive hemorrhages. The peritoneum may be bright red in color and the omentum may show extensive hemorrhages. The mucous membranes of the larynx, trachea, and bronchi are bright-red in color (or black-red if smoke has been inhaled) and may be covered with a viscous, thick, frothy mucous. Ecchymoses may be found in the heart and lungs. The kidneys may show fatty degeneration and necrosis in the convoluted tubules.

The brain and meninges show a marked hyperemia and, not infrequently, there is edema, especially in the medulla and pons. The ventricles and arachnoid space contain a rather large amount of watery or blood-tinged fluid. Punctiform hemorrhages and softening in the cortex and central nuclei of the brain, especially in the two internal

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[1] See *Lehrbuch der gerichtlichen Medizin* by Hofmann-Haberda, 11te. Aufl., 1927, p. 875 for accounts of such cases.

[2] Guy's Hosp. Rep., 1889, **46**, 223.

[3] Jour. Ind. Hyg., 1921, **3**, 213.

[4] See Hedinger, Vrtljschr. f. ger. Med., 1920, **59**, 172 and Virchow's Arch., 1923, **246**, 412; Riedel, Deutsch. med. Wchnschr., 1921, **47**, 651; Hofmann-Haberda, *Lehrbuch der gerichtlichen Medizin*, 11te. Aufl., 1927, p. 876.

segments of the lenticular nucleus (*globus pallidus*), where the degenerations are symmetrical, are rather frequent and characteristic.[1] There may be foci of necrosis about the distribution of the sylvian arteries.[2] The pia of the spinal cord may be markedly hyperemic, while localized edema and punctiform hemorrhages may be observed. A diffuse degenerative process develops in the nerve cells, especially those in the extrapyramidal motor tract and in the anterior horn of the cervical and dorsal cord, less commonly in the lumbar and sacral cord, these[3] changes being accompanied by a reactive proliferation of the gliosa cell elements.

Detection.—While the bright cherry-red color of the blood, the red spots on the skin, the bright red color of the muscles and the viscera point to possible carbon monoxide poisoning, this is made certain only by examination of the blood, and, if possible, the examination of the air which the victim may have inhaled. The tests of the blood are of special importance as the carboxy-hemoglobin remains detectable for long periods even in the presence of marked putrefaction. If the tube containing such blood be tightly stoppered, the carboxy-hemoglobin can be detected after the lapse of several years.

In the Blood.—The methods employed for detection of carboxy-hemoglobin are (1) spectroscopic and (2) chemical, the former being somewhat more delicate and sensitive, especially if a microspectroscope be used.

1. *Spectroscopic Tests.*—In testing blood for the various absorption spectra, it must be strongly diluted, ½ to 1 cc. being diluted to 100 cc. with distilled water. Blood which has been dried at room temperature will show these spectra almost as well as fresh blood.

Blood containing carboxy-hemoglobin shows a characteristic absorption spectrum, which closely resembles that of oxyhemoglobin (See Plate I.). In both cases there are two absorption bands in the yellow and green portions of the spectrum between the Fraunhofer lines D and E, the band near D being the narrower of the two and lying, in each case, in practically the same position. The broader band of the carboxy-hemoglobin spectrum is nearer the line E than is that of oxyhemoglobin and the space between the two absorption bands of carboxy-hemoglobin is greater than that between the oxyhemoglobin bands.

As these two spectra are so similar, it is not the simplest matter to differentiate them in all cases. Fortunately, however, we have a further test which will clear up any doubt that may exist. If normal blood, that is one containing oxyhemoglobin, be diluted and examined spectroscopically, the two lines of oxyhemoglobin stand out clearly. If there be added to this solution a drop or two of freshly prepared ammonium sulphide solution or of Stokes' solution of ammoniacal ferrotartrate, the oxyhemoglobin is reduced to hemoglobin and the absorption spectrum will change, showing one broad clearly defined band between D and E, lying toward the red end of the spectrum a little over the Fraunhofer line D and occupying about ⅔ of the space to the E line. If, however,

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[1] See Kolisko, Beitrage zur gerichtlichen Medizin, 1914, 2; Hofmann-Haberda, *Loc. cit.*, p. 884.

[2] See Norris, Ind. Hyg. Bull., New York State Dep't of Labor, 1925, **2**, 1.

[3] See Lewin, *Die Kohlenoxydvergiftung*, 1920; Grünstein and Popowa, Arch. f. Psych. und Nervenkrankheiten, 1928, **85**, 283.

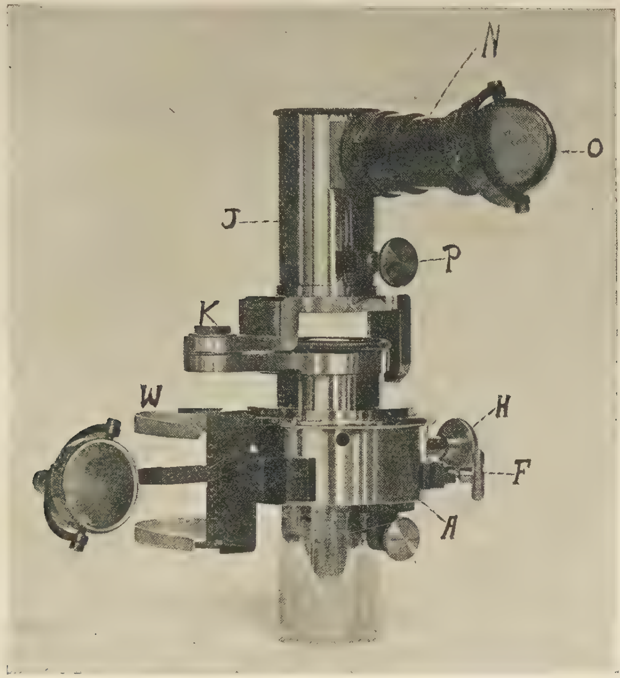

FIG. 46.—The microspectroscope. The instrument may be used for the detection of small quantities of blood in solution and is very useful in the detection of carbon monoxid hemoglobin. The instrument consists of two main divisions, the drum (*A*) which fits into the tube of the microscope and the spectroscope (*J*). The drum contains an adjustable slit worked by the screws (*H*) and (*F*) which controls the length and breadth of the ray of light which comes to the eye from the object. By means of the screws the spectra are properly focussed. The drum also contains a prism illuminated by a side mirror, and moved into or out of the field by a projecting lever. With this mirror is a clamp to hold a small tube of solution which it may be desired to test or which may be used to give a comparison spectrum. The spectroscope (*J*) revolves on the pivot (*K*), so that it can be brought into position over the eye-piece or moved away to permit focussing the object. At the side is a tube (*N*) which contains a scale, the divisions of which represent wave lengths, expressed in one hundred thousandths of a millimeter. By means of the mirror (*O*) the scale is thrown upon the spectrum of the object, and it is focussed by the sliding tube (*N*). It should be adjusted by the sliding screw (*P*) so that Fraunhofer's line (*D*), the sodium line, coincides with the division line 58.9, the wave length of the sodium line being 589 millionths of a millimeter. A small test-tube of known solution is placed in the clamps (*W*) at the side of the drum and compared with the unknown solution in a cell of 1 c.c. capacity, mounted on a glass slide on the stage of the microscope. The drum prism furnishes a comparison spectrum. (Doremus and McNally, in Peterson, Haines and Webster, "Legal Medicine and Toxicology.")

the spectrum first noted be due to carboxy-hemoglobin instead of to oxyhemoglobin, the addition of reducing agents does not convert the spectrum into one of hemoglobin, so that the two bands of carboxy-hemoglobin will still persist. Unfortunately, this differentiation is not always as clear as it may seem. If the blood, when it is examined, contains less than about 30 per cent of carboxy-hemoglobin, the addition of the reducing agent will, of course, reduce the oxyhemoglobin present to hemoglobin and the resulting spectrum may be very confusing. In such cases, however, the broader band of the carboxy-hemoglobin spectrum, being located nearer E than is the band of hemoglobin, will persist and may be detected by careful study. Banham, Haldane and Savage[1] state that the possible presence of nitric acid hemoglobin must always be considered in cases of suspected CO poisoning, and recommend boiling the diluted blood, when a pink coagulum results if nitric oxide is present.

2. *Chemical Tests.*—Practically all of the chemical tests used for detection of carbon monoxide in blood depend upon the precipitation of protein which carries with it the carboxy-hemoglobin and, thus, forms a distinct precipitate in contrast to the coloration produced with normal blood. There are many of these tests, but we shall limit ourselves to those which seem to yield most satisfactory results.

(*a*) *Sodium Hydroxide Test.*—This test, originated by Hoppe-Seyler, is performed by mixing the suspected blood in a porcelain dish with an equal or a double volume of caustic soda solution (sp. g. 1.3), when normal blood forms a black, gelatinous mass which appears greenish-brown in thin layers; while blood containing carboxy-hemoglobin, in as low concentrations as 0.1 per cent., forms a red coagulum.

(*b*) *Katayama's Test.*—This test is a modification and improvement of an earlier test of Salkowski. The suspected blood is diluted with water in the proportion of 1 to 50. Of this dilution, place 10 cc. in a test-tube and add 0.2 cc. of orange colored ammonium sulphide solution[2] and 0.2 to 0.3 cc. of 30 per cent. acetic acid to faintly acid reaction. Mix and filter off the precipitated sulphur, when the filtrate will remain red if carbon monoxide is present, while the color of normal blood will be a dirty, dark green or gray.

(*c*) *Welzel's Test.*—Dilute the blood with four volumes of distilled water and add three volumes of a 1 per cent. solution of tannic acid, and shake the mixture thoroughly. Normal blood gives a gray precipitate (especially after standing for some hours), while carbon monoxide blood yields a carmine-red precipitate. These differences in color become more marked on standing, while the red color of the CO blood persists for years. According to Witthaus[3], carbon monoxide blood diluted with normal blood 1:12 responds to this test. Other precipitants have been used by Welzel, in conjunction with Kunkel, such as zinc chloride, mercuric chloride, platinic chloride, phosphomolybdic acid, picric acid, potassium ferrocyanide and acetic acid, and phenylhydrazine, but the tannic acid mixture seems to yield the most satisfactory results. This test of Welzel is, possibly, the best of the precipitating tests to use as a routine as it invariably shows the presence of carbon monoxide, except when this is present in very low concentrations, and yields positive results with blood taken from bodies embalmed with formaldehyde. As Fishbein[1] has shown many of these tests either do not react positively or are obscured by the presence of formaldehyde.

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[1] Brit. Med. Jour., 1925, **2**, 187.

[2] This solution is prepared by adding 1 to 2 grams of sulphur to fresh colorless or yellow ammonium sulphide solution.

[3] *Toxicology*, 1911, p. 1136.

(*d*) *Rubner's Test.*—Add 4 or 5 volumes of basic lead acetate solution to the blood and shake thoroughly for a minute or so. Carbon monoxide blood gives a red color, while normal blood yields a brownish changing to a brownish-gray color. The differences in color increase on standing and persist for some months. In the presence of formaldehyde this test yields a whitish coagulum.

(*e*) *Liebmann's Test.*—In view of the fact that formaldehyde interferes with the above tests, with the exception of Welzel's test, it is interesting to note that Liebmann finds that addition of formaldehyde to normal blood produces a dirty brown color, while with carbon monoxide blood the usual red color persists for weeks. This fact is of importance as it permits the recognition of the reddish color of the internal organs after the body has been embalmed with formaldehyde.

In the Air.—The tests employed for detection of carbon monoxide in the air are based partly on the formation of carboxy-hemoglobin and its spectroscopic or chemical identification and partly on the reducing action of carbon monoxide upon certain metallic compounds. In certain cases advantage is taken of the action of the gas upon mice and birds as an indication of a dangerous atmosphere.

Vogel recommends the shaking of a liter or more of the suspected air in a bottle to which has been added 5 to 10 cc. of strongly diluted normal blood, when the carboxy-hemoglobin formed is identified by the spectroscope. Hempel modifies this method by drawing by aspiration 10 liters or more of air through 10 cc. of diluted blood contained in a small flask and the later spectroscopic examination of the blood, by which method he was able to detect CO in amounts of 0.05 per cent. This method may be made still more delicate by freeing the air of its oxygen, as recommended by Zuntz and Kostin, by filling large bottles, containing iron wire gauze moistened with ammonia water, with the suspected air, shaking and allowing to stand for ½ hour. The air in the bottle is then aspirated through dilute sulphuric acid to remove any ammonia and is then drawn through the blood solution as in Hempel's method.

Carbon monoxide has the power of reducing palladous chloride to palladium. Advantage is taken of this fact by exposing strips of filter paper saturated with a neutral yellowish-red solution of palladous chloride to the action of the suspected air contained in a large bottle. If filter paper saturated with even such a dilute solution as 0.2 per cent. palladous chloride be hung in a 10 liter bottle of the suspected air, 0.5 part of CO per 1000 of air will blacken the paper in a few minutes, 0.1 part per 1000 in 2 to 4 hours and 0.05 part per 1000 in 12 to 24 hours. It is preferable, however, to use somewhat stronger solutions of the palladous chloride, Desgrez and Labat[1] recommending a 10 per cent solution. This method is open to the objection that other substances, such as hydrogen sulphide, ozone, and sulphurous acid, will also darken the palladous chloride paper. For this reason the test, applied as above, is of more importance in its negative than in its positive phase. If this preliminary test should prove positive, it is wise to use the following procedure. Through a solution of ammoniacal cuprous chloride aspirate the suspected air, which is first washed through a solution of lead acetate to remove any hydrogen sulphide present, when the copper solution absorbs the CO present. Now pour this solution slowly into a neutral bright red solution of palladous chloride, when a black precipitate of metallic palladium will come down, or, if only a small amount of CO be present, a darkening of the solution will occur.

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[1] Jour. Amer. Med. Assoc., 1913, **60**, 737.

Hoolamite Method.—Hoover[2] recommends the use of hoolamite (an activated iodine pentoxide indicator consisting of fuming sulphuric acid, iodine pentoxide and pumice stone) for detection of CO. When this material is exposed to the air a green color develops in the presence of CO, the depth of the color varying with the concentration in the air. Concentrations of CO as low as 0.07 per cent show positive results with this reagent. The color fades from the material after a time, except when the concentration is high, so that hoolamite may be used several times before being exhausted, providing it is kept in closed containers when not in use for tests.[3]

Physiologic Tests.—It has been shown by experiments that white mice and canaries are more quickly affected by carbon monoxide than are men. For this reason it has been recommended that the air in mines and other places where men are working in vitiated air should be tested by placing, in the suspected air, cages containing these animals and observing the effects. Canaries seem to be preferable to mice as they show symptoms earlier and are easier to observe. As a rule these birds show signs of distress when exposed to concentrations of 0.1 per cent CO for 60 minutes, to 0.15 per cent. for 5 to 30 minutes, to 0.2 per cent.

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[1] Ann. chim. et anal. chim. appl., 1919, **1**, 294.

[2] Jour. Ind. and Eng. Chem., 1921, **13**, 770. See, also, Katz and Bloomfield, Ibid., 1922, **14**, 304; Sayers and Yant, Reports of Investigations, Serial No. 2478, Bureau of Mines, 1923.

[3] The Mine Safety Appliances Co., 908 Chamber of Commerce Bldg., Pittsburgh, Pa., has placed on the market the M-S-A Carbon Monoxide Detector, which permits of a rapid and relatively accurate quantitative as well as qualitative test of the CO in the air. The detector is simple in construction and may be recommended for routine testing of air.

for 2 to 5 minutes, and to 0.25. per cent in 1 minute, falling from their perch in 3 minutes.[1]

Determination.—Several of the older methods of determination of the carbon monoxide in the blood of the victims of poisoning yield satisfactory results, but we shall simply mention these by name as the methods of Fodor[2], Haldane[3] and Nicloux[4]. The newer methods are somewhat simpler and are just as exact.

Pyro-Tannic Acid Method[5].—This is a modification of the method of Sayers and Yant[6] in the sense that permanent color standards have been prepared and the apparatus has been remodeled and compactly arranged in a pocket case. By the use of this method the presence of CO in the blood may be detected in 3 minutes and a determination of the exact amount may be made within 15 minutes. This test is based on the tannic acid qualitative test previously discussed, in which a light brownish gray suspension is formed after a few minutes when normal blood diluted with water is treated with a solution of tannic and pyrogallic acids and light carmine suspensions are formed with blood having CO in combination with all of its hemoglobin, while in a mixture of normal blood containing CO the suspension formed will be a corresponding mixture of the two extremes of color. By comparing the color formed in the reaction with a set of standards, the amount of CO in the blood may be readily determined.[7]

Technic.—A small puncture wound is made with a blood needle in the tip of the finger or the lobe of the ear of the victim. If death has occurred it will probably be necessary to obtain the blood by puncture of a vein. By means of the pipet (the capillary stem of which is calibrated to a 0.1 cc. mark and the total capacity of the pipet is 2 cc., thus permitting a dilution of 1: 20) draw the blood up to the 0.1 cc. mark, wiping off any excess on the outside of the pipet just as when making a blood count, and then draw distilled water into the pipet until the mixture reaches the 2 cc. mark. This diluted blood is then discharged into one of the small test-tubes and the pipet washed out by sucking the mixture back into the pipet once or twice and expelling it completely. Immediately after the blood solution has been discharged into the test-tube add the contents of one capsule (containing 0.04 gram of a 1: 1 mixture of tannic and pyrogallic acids) and invert the tube three or four times to insure thorough mixing. Place this tube in the rack and allow it to stand for 15 minutes at room temperature. At the end of this time compare the color of the unknown with the standards, using daylight but not direct sunlight, by interposing the tube between the standards until the one which it most nearly matches is found. The percentage of carboxy-hemoglobin is then read off from the value of the matched standard. As a blood saturated with carbon monoxide holds in combination 20 per cent. by volume of this gas, it follows that the percentage of saturation, or in other words the coefficient of poisoning with carbon monoxide,[1] may be easily determined by dividing the percentage of carbon monoxide per 100 cc. of blood by the percentage (20) such blood will contain when the hemoglobin is completely saturated.

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[1] See Haldane, Colliery Guardian, 1909, **98,** 1251; Burrell, Technical Paper 11, Bureau of Mines, 1921; Burrell, Seibert and Robertson, Technical Paper 62, Bureau of Mines, 1913; Burrell and Oberfell, Technical Paper 122, Bureau of Mines, 1915.

[2] Deutsch. Vrtljschr. f. off. Gesundhtspfl., 1880, **12,** 377.

[3] Jour. Physiol., 1895, **18,** 430 and 463; Ibid., 1896, **20,** 521.

[4] C. R. Acad. d. sc., 1898, **126,** 746; Bull. soc. chim. biol., 1920, **2,** 171; Ibid., 1921, **3,** 286.

[5] Sayers, Yant and Jones, Pub. Health, Rep., 1923, **38,** 2311.

[6] Jour. Amer. Med. Assoc., 1922, **78,** 1745.

[7] The complete apparatus for this test may be obtained from the Mine Safety Appliances Co., 908 Chamber of Commerce Bldg., Pittsburgh, Pa.

If it is desired to determine the amount of CO in the air by this method, proceed as follows: Obtain a sample of the air by inserting the glass tube on the end of the scrubber into a 250 cc. sample bottle, and then aspirate the air through the sample bottle long enough to remove the original air in the bottle, which will require at least 25 squeezes of the bulb. Insert the rubber stopper quickly and tightly. When the specimen of air reaches the laboratory, obtain 0.1 cc. of blood from a person who has not been exposed to CO and dilute this as mentioned above to 2 cc. in the special pipet. Now discharge this diluted blood at once into the sample bottle containing the suspected air and replace the stopper. Rotate the bottle horizontally and constantly for 15 to 20 minutes, avoiding violent shaking but covering as much as possible of the surface of the bottle with the blood solution. When equilibrium has been established between the oxyhemoglobin and the carboxy-hemoglobin, the blood solution is poured into a small test-tube and the tannic-pyrogallic acid mixture added as in the test previously discussed. The amount of carboxy-hemoglobin formed is then read off from the standards. The calculation of the amount of CO in the air is then made from the following equation:

$$P_{co} = \frac{\text{COHb}}{100 - \text{COHb}} \times \frac{2093}{300}$$

In which P_{co} equals parts of CO per 10,000 of air; COHb equals percentage saturation as found by analysis; 2093 equals oxygen content of normal air in parts per 10,000; and 300 equals the average relative affinity of hemoglobin for carbon monoxide as compared with its affinity for oxygen. Thus, if a blood solution brought into equilibrium with a gas sample was found to contain 60 per cent. of COHb by this test, by substitution in the equation we obtain

$$P_{co} = \frac{60}{100 - 60} \times \frac{2093}{300} = 10.4 \text{ parts per } 10{,}000$$

Van Slyke and Salvesen's Method.—The principle of this method[2] is to set free the oxygen and carbon monoxide from their combination with hemoglobin in the blood by addition of ferricyanide and then to remove both gases with the help of a Torricellian vacuum in the apparatus devised by Van Slyke for determining the CO_2 combining power of the plasma.[1] The oxygen is absorbed in the apparatus by alkaline pyrogallate and the volume of residual carbon monoxide is measured directly at atmospheric pressure, a correction being made for the small and constant amount of nitrogen gas physically dissolved in the blood. The work of O'Brien and Parker[2] indicates that the amount of CO dissolved in the serum is so small that there is little to be gained by making a correction for this factor.

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[1] See Simonin, Ann. de méd. lég., 1929, 9, 11.

[2] Jour. Biol. Chem., 1919, **40**, 103. See, also, Van Slyke and Robscheit-Robbins, Ibid., 1927, **72**, 39.

The blood-gas apparatus is prepared by introducing into it 5 drops of redistilled caprylic alcohol and 6 cc. of ammonia solution made by diluting 4 cc. of concentrated ammonia to a liter. If saponin powder is available, as much is added to the 6 cc. of ammonia, while in the cup of the apparatus, as will stick to the end of a glass rod (approximately 1 mg. per cc.). After the ammonia is introduced into the 50 cc. chamber of the apparatus, the latter is evacuated and the air is extracted from the ammonia solution by shaking for about fifteen seconds. The extracted air is expelled, and the extraction repeated to make sure that no air is left in the solution. Finally, about 2 cc. of the air-free ammonia are forced up into the cup of the apparatus. The blood of the victim of poisoning is drawn by venous puncture and should be oxalated to prevent clotting. Draw into a pipet a 2 cc. sample of the well mixed oxalated blood and run it under the ammonia in the cup of the apparatus. Allow the blood to run from the cup into the 50 cc. chamber, the ammonia layer following the blood and washing it in. The blood and ammonia in the chamber are mixed and allowed to stand until the blood is completely laked, a process requiring about 30 seconds if saponin be present and 5 minutes if it is not. After the laking is complete, 0.4 cc.

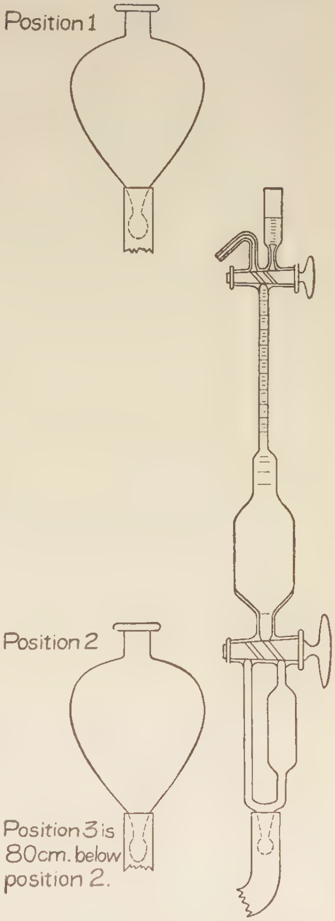

FIG. 47.—Van Slyke's apparatus for carbon dioxid of blood, showing the three positions of the mercury bulb. The bulb is connected to the apparatus by a heavy rubber tube which is merely indicated in the drawing. The apparatus is set up on an iron ring stand. (Todd and Sanford.)

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[1] Ibid., 1917, **30**, 289 and 347.

[2] Jour. Biol. Chem., 1922, **50**, 289.

of a saturated potassium ferricyanide solution is introduced to set free the oxygen and carbon monoxide combined with the hemoglobin.[1] The apparatus is now evacuated by lowering the leveling bulb until only a few drops of mercury remain above the lower stopcock, and is shaken, preferably with a rotary motion, to whirl the blood into a thin layer around the wall of the chamber. If the blood was completely laked before the addition of the ferricyanide, extraction of the gases may be completed by half a minute of efficient shaking. The extracted solution may be drawn into the lower bulb below the stop-cock and the extracted gas measured over mercury. When the reading of the volume of the gas mixture, consisting of oxygen, carbon monoxide, and a little nitrogen is constant, a solution of alkaline pyrogallate[2] is introduced into the cup of the apparatus, is covered with a thin layer of paraffin oil, and is allowed to flow slowly down the inner wall of the graduated part of the apparatus. A little suction is produced during this part of the procedure by lowering the leveling bulb slightly. The absorption of the oxygen is quite rapid and is completed in less than one minute; the reading is taken and the pyrogallate solution introduced once more until a constant reading is obtained. The remaining gas, consisting of CO and N_2, is then measured under the conditions of prevailing pressure and temperature. As the solution is very dark and it is a little difficult to get good readings of the meniscus, a new meniscus is produced by letting water flow down after the pyrogallate solution, the water floating on top of the fluid and permitting readings to about 0.002 cc. After the determination the apparatus should be carefully washed out with dilute ammonia solution.

The gas measured is reduced to standard conditions by multiplying by the factor $(0.999 - 0.0046\,t) \times \frac{\text{barometer}}{760}$, t being the observed temperature in degrees C. If 2 cc. of blood have been used, as directed in the test, the values of this factor may be found by reference to the following table, the result then being expressed in cc. of CO per 100 cc. of blood, from which amount the nitrogen correction, 1.2, must be subtracted. As a saturated blood holds in combination 20 per cent. of CO by volume, the degree of saturation may be obtained by a simple calculation.

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[1] This ferricyanide solution is prepared by dissolving 40 grams of the salt in 100 cc. of water and is made air-free by boiling or shaking in an evacuated flask and is kept in a buret under a layer of paraffin oil 2 or 3 cm. thick to exclude air.

[2] This is prepared by dissolving 10 grams of pyrogallic acid in 200 cc. of strong potassium hydroxide (160 grams KOH dissolved in 130 cc. of water).

Temperature, ° C.	*Factor by which observed gas volume is multiplied in order to give carbon monoxid in 100 c.c. of blood*
15	$46.5 \times \frac{B}{760}$
16	$46.3 \times \frac{B}{760}$
17	$46.0 \times \frac{B}{760}$
18	$45.8 \times \frac{B}{760}$
19	$45.6 \times \frac{B}{760}$
20	$45.4 \times \frac{B}{760}$
21	$45.1 \times \frac{B}{760}$
22	$44.9 \times \frac{B}{760}$
23	$44.7 \times \frac{B}{760}$
24	$44.4 \times \frac{B}{760}$
25	$44.2 \times \frac{B}{760}$
26	$44.0 \times \frac{B}{760}$
27	$43.7 \times \frac{B}{760}$
28	$43.5 \times \frac{B}{760}$
29	$43.3 \times \frac{B}{760}$
30	$43.1 \times \frac{B}{760}$

Instead of measuring the carbon monoxide and nitrogen as outlined above and making a correction for the nitrogen, one may absorb the carbon monoxide and measure the remaining nitrogen, which will show the exact amount of CO present. In this procedure, which is a part of the modification of the previous method introduced by O'Brien and Parker[1], rinse out the cup of the apparatus with distilled water to remove any pyrogallate left behind, removing the wash water by means of a small dropping pipet. Now add 0.5 to 1 cc. of an ammoniacal cuprous chloride solution[2], allowing it to flow into the apparatus just as was the case with the pyrogallate. The CO is quickly absorbed and a constant volume obtained almost immediately. If the remaining gas (nitrogen) be measured and subtracted from the previously read volume of the mixture of CO and N_2, the amount of CO absorbed is obtained. This amount is then corrected for temperature and barometric pressure as previously stated and, by using the factor as given in the table, the percentage of CO by volume is obtained.

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[1] Jour. Biol. Chem., 1922, **50**, 289.

[2] This solution is prepared by dissolving 400 grams of cuprous chloride and 500 grams of ammonium chloride in 1500 cc. of water. For use this is mixed with ammonium hydroxide (sp. g. 0.9) in proportions of 3:1.

HYDROGEN SULPHIDE

(Sulphuretted Hydrogen, "Stink Damp")

Hydrogen sulphide is a product of the putrefaction of organic substances containing sulphur, and is found, therefore, in cesspools, sewers[1], privy vaults, tannery vats[2], fat rendering plants, and glue factories. It is also generated[3] by decomposition of organic matter by anerobic bacteria in deep lakes and ponds, while streams receiving city sewage are highly contaminated with this gas. It is found naturally in volcanic regions, spring waters in the neighborhood frequently becoming impregnated with it. It is liberated in such industrial processes as the making of dyes, manufacture of sulphur monochloride, and preparation of barium carbonate from the sulphide, while it is a frequent contaminant of the air of laboratories from decomposition of metallic sulphides by acids. This gas is not infrequently found in the air of mines (stink damp) and is formed in the distillation of petroleum oil containing sulphur, in the handling of slags, and as a contamination of illuminating and heating gas. This gas is one of the products of putrefactive processes in the human body, especially in the intestine, and may produce indefinite symptoms of auto-intoxication when absorbed.

Hydrogen sulphide is a colorless, transparent gas having a strong, penetrating, nauseating and irritating odor of rotten eggs. It is readily soluble in water, this solution gradually decomposing with the deposition of white sulphur. It is combustible, burning with a blue flame and producing water and sulphur dioxide. When mixed with ½ its volume of oxygen and ignited, H_2S explodes with a deposition of sulphur, while 2 volumes of H_2S and 3 of O_2 yield sulphur dioxide on explosion. It is slightly heavier than air, its specific gravity being 1.1912. One liter of this gas at 0°C. and 760 mm. pressure weighs 1.52 grams.

Poisoning with this gas may occur in chemical laboratories, in which work is more or less constantly being carried out with H_2S, in industrial plants in which large quantities of the gas may be liberated in the course of various manufacturing processes, and in those places in which the air is markedly contaminated with sewer gas. This latter gas is a mixture of various gases, such as nitrogen, carbon dioxide, hydrocarbons, ammonia, hydrogen sulphide, and air, the greatest danger being from the sulphide, although in some cases the symptoms may be largely traceable to lack of oxygen in the respired air. Illuminating gas contains some hydrogen sulphide, but the effects of this gas are largely due to the presence of carbon monoxide.

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[1] See Klein, Deutsch. Ztschr. f. d. ges. gerichtl. Med., 1922, **1**, 228.

[2] See Tauss, Zentralbl. f. Gewerbehyg., 1920, **8**, 74; and Myers, Jour. Bact., 1920, **5**, 231.

[3] See "Hydrogen Sulphid" by Doremus and McNally in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 336.

Action.—Hydrogen sulphide is both an irritant and a systemic poison. When it is brought in contact with the moist respiratory tissues, it combines with the alkali present forming sodium sulphide, irritation resulting both from the withdrawal of alkali from the tissues and from the caustic action of the sulphide. A portion of this alkali sulphide is absorbed from the alveoli and enters the blood stream, where it is hydrolyzed with the liberation of hydrogen sulphide. In the presence of the oxygen of the blood, this H_2S is rapidly oxidized to sulphuric acid which then combines with the alkalies of the blood forming harmless sulphates.[1] This irritant action is accountable for the respiratory and ocular symptoms which may be very prominent. Besides this irritant action, hydrogen sulphide shows an immediate systemic action, if the concentration is sufficient, which is exerted largely upon the central nervous system and which is accountable for the more or less sudden deaths which are encountered.

Hydrogen sulphide is commonly supposed to combine with oxyhemoglobin to form sulphemoglobin or, more accurately speaking, sulphmethemoglobin. It has, however, been shown by Haggard[2], that no such combination is ever found in the body after hydrogen sulphide poisoning providing the autopsy is performed soon after death. As pointed out by Haggard, this gas combines only with methemoglobin and not with oxyhemoglobin, so that no sulphur compound is formed with the hemoglobin as a result of the inhalation of the gas, because methemoglobin is not normally present in the blood. It seems clear, therefore, that this sulphmethemoglobin can be formed only in the relatively rare conditions in which the oxyhemoglobin is reduced to methemoglobin. If, however, there is some delay in performing the autopsy, processes of putrefaction set in, and, under these conditions, an abundant formation of this sulphmethemoglobin may be noted solely as a postmortem change and not as an indication of a previous hydrogen sulphide poisoning. Kobert[3] believes that there is some formation of sulphmethemoglobin in cases of acute H_2S poisoning, but that this must be detected by chemical means, as the spectroscopic tests are not sensitive enough for such purposes. It must be remembered, in this connection, that there are occasional cases in which sulphmethemoglobin may be found in the blood when there has been no exposure to hydrogen sulphide, its formation being due to the production of methemoglobin and its combination with small amounts of H_2S arising from the digestive tract.

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[1] See Henderson and Haggard, *Noxious Gases*, 1927, p. 189; Denis and Reed, Jour. Biol. Chem., 1927, **72,** 385; Fowler, Oil and Gas Jour., 1928, **26,** 170 and 173.

[2] Jour. Ind. Hyg., 1925, **7,** 113. See, also, Balthazard and Sava, Ann de méd. lég. de criminol. et de police scient., 1928, **8,** 1.

[3] Lehrbuch der Intoxikationen. 2te. Aufl., 1906, **2,** 832.

Such cases have been especially described by van den Bergh[1], who calls the condition "idiopathic enterogenous cyanosis".

Symptoms.—When hydrogen sulphide is breathed in a concentrated form, death is almost immediate from respiratory failure due to paralysis of the respiratory center, the action being as rapid as that due to high concentrations of carbon monoxide or of hydrocyanic acid. In acute poisoning the symptoms observed depend both upon the concentration of the gas and the time of exposure, the action being manifested only while there is free hydrogen sulphide in the blood. Concentrations of the gas higher than 2000 parts per million (0.2 per cent.) cause almost immediate cessation of breathing, while concentrations between 600 and 2000 parts per million cause hyperpnea through stimulation of the respiratory center, the excessive breathing lowering the carbon dioxide content of the blood and apnea resulting.[2]

If the gas be inhaled in concentrations not sufficient to produce rapidly fatal results, the symptoms comprise nausea, possibly vomiting, headache, giddiness, cold skin, dyspnea, irregular cardiac action, occasionally auricular fibrillation, and death in coma associated with violent tetanic convulsions in some cases. "In small amounts the sulphide depresses the nervous system; in larger amounts it stimulates, and in very large amounts it paralyzes the nervous system." In very low concentrations drowsiness is produced, which may extend into unconsciousness and death if the inhalation be continued sufficiently long. In the subacute cases of poisoning the main symptoms noted are those of irritation of the respiratory tract, this leading in some cases to pulmonary edema and death in a few days, and of the eye. Although in acute cases the symptoms of irritation may be obscured by those of the systemic action, yet one may observe erosion of the surface of the epithelium, the irritation being more or less limited to the surface, and photophobia, while conjunctivitis (pink eye) may occasionally be seen.[3] While the symptoms of acute poisoning develop, as a rule, immediately on the inhalation of the gas, yet there may be cases in which the symptoms do not appear until after the pause of a few hours, when nausea, weakness, headache, dizziness, pains in the abdomen, drowsiness, and disturbed respiration may be noted.[4]

While hydrogen sulphide is a strictly non-cumulative poison, revived victims usually suffering no systemic sequelae, yet there is, possibly, a distinct chronic type of poisoning from H_2S in those daily exposed to its action. These workers complain of irritation of the eyes, headache, constipation, anemia, and malaise. There does not appear to be any tolerance established for this gas, but, on the contrary, an increased sensitiveness to it seems to develop.[1]

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[1] Deutsch. Arch. f. klin. Med., 1905, **83,** 86; Berl. klin. Wchnschr., 1906, **43,** 7.

[2] See Haggard, Jour. Pharm. and Exp. Therap., 1922, **19,** 262 and Jour. Ind. Hyg., 1925, **7,** 113; Henderson, Haggard and Charlton, Amer. Jour. Physiol., 1922, **61,** 289; Henderson and Haggard, *Noxious Gases,* 1927, p. 190.

[3] See Clark, Med. Jour. Australia, 1924, **1,** 439.

[4] See Kobert, *Lehrbuch der Intoxikationen,* 2te. Aufl., 1906, p. 30.

Lethal Dose and Period.—It has been found that, after an exposure of several hours to a concentration of 100 to 150 parts of H_2S per million, only slight symptoms are shown; that a concentration of 200 to 300 parts per million is the maxium amount that can be inhaled for 1 hour without serious disturbance; that a concentration of 500 to 700 parts per million is dangerous if inhaled for 30 minutes to 1 hour; while a concentration ranging from 1000 to 3000 parts per million (0.1 to 0.3 per cent.) is rapidly fatal.[2] The limit of danger for prolonged exposure is said to be a concentration of 50 parts per million (0.005 per cent.) or possibly lower.[3]

Treatment.—As death from hydrogen sulphide is due to respiratory failure, measures should be adopted to stimulate and restore natural breathing. The patient must be removed to fresh air as quickly as possible, but, as Henderson and Haggard state, spontaneous breathing can not be expected to return after the paralytic form of respiratory failure. After the overstimulated form of failure, however, breathing may return spontaneously, but this is hastened by the use of artificial respiration (see p. 561) and inhalation of oxygen mixed with 5 per cent. of carbon dioxide. The heart continues to beat for some minutes after the respiratory failure. After spontaneous breathing has been restored, the treatment should be symptomatic and supportive. The prophylaxis of hydrogen sulphide poisoning consists in keeping the contamination of the air at a low level by means of forced ventilation. Workers exposed to this gas should wear suitable masks (such as the "all service mask") or a self-contained breathing apparatus (discussed under carbon monoxide) and should wear goggles to protect the eyes.

Postmortem Appearances.—There are no distinctive anatomic changes in hydrogen sulphide poisoning. In rapidly fatal cases, the signs found are simply those of asphyxia. If death has been delayed for a few days, evidences of edema of the lungs is present. There may be marked rigor mortis and the muscles may have a dark color and are not responsive to electric stimulation. If there is some delay in performing the autopsy, a bluish-green color of the blood may be observed, due to the formation of sulphmethemoglobin. This change in the color of the blood is especially noticeable in the vessels surrounding the intestines and, occasionally, in the brain.

Detection.—The recognition of a case of poisoning from hydrogen sulphide is based largely on the detection of this gas in the air to which the victim has been exposed. Ordinarily the amount of H_2S in the fresh corpse is too small to give satisfactory results, while examinations of the body that has undergone putrefaction is useless as the decomposition processes produce so much of this gas that nothing of forensic value is forthcoming.

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[1] See Rodenacker, Zentralbl. f. Gewerbehgy. u. Unfallverhüt, 1927, **14,** 205.

[2] See Kobert, *Loc. cit.;* Haggard, Jour. Pharm. and Exp. Therap., 1922, **19,** 262; Sayers, Reports of Investigations, Serial No. 2491, Bureau of Mines, 1923.

[3] Haggard and Henderson, *Noxious Gases,* 1927, p. 191.

In the Air.—The odor of hydrogen sulphide is highly characteristic and is, often, more penetrating in low concentrations, so that this characteristic may be taken advantage of in detecting its mere presence in the air. If a piece of filter paper be moistened with a solution of lead acetate and then be exposed to the suspected air, a brown or black coloration or precipitate will appear on the paper in the presence of hydrogen sulphide. A further test, which is quite delicate, is the following: Conduct several liters of the suspected air through a dilute solution of ammonia containing a few drops of dilute sodium nitro-prusside solution, when a violet coloration will appear in the presence of traces of hydrogen sulphide. Probably the most delicate test for H_2S, either in the air or in solution, is that of Caro-Fischer. Conduct the suspected air through water and treat the aqueous solution with $1/50$ of its volume of fuming hydrochloric acid. Now add a few crystals of para-amidodimethylaniline hydrochloride and, after these have dissolved, add 1 or 2 drops of a dilute solution of ferric chloride. In the presence of hydrogen sulphide, the solution becomes gradually blue from the formation of methylene blue, the reaction being sensitive in the presence of 0.000009 to 0.000018 gram of H_2S per liter.[1]

In the Blood.—As previously stated hydrogen sulphide is rarely, if ever, present in the blood of a fresh corpse poisoned with the gas, so that examinations are rarely of value. If the tissues and blood are obtained at a late autopsy, the blood may show evidences of the presence of this gas in the bluish-green color and in the spectroscopic tests. This test is far from characteristic as it is not delicate enough to detect the small amounts which may, possibly, be present. The spectrum of sulphmethemoglobin, if such be observed, is shown by the presence of two bands, one in the red midway between C and D, the other fainter beginning at D and extending over half-way to E.

The quantitative determination of the amount of hydrogen sulphide in the air is rarely of importance in forensic cases, although occasionally it may be desirable to carry out such an estimation. For these methods I refer to the literature.[2]

HYDROGEN ARSENIDE

(Arseniuretted Hydrogen; Arsine)

Hydrogen arsenide (AsH_3) is a very subtle and powerful poison, and is produced whenever nascent hydrogen is formed in the presence of a soluble or reducible compound of arsenic. Most metallic ores contain arsenic, which is not removed in the course of the usual metallurgical processes of smelting and refining, so that the ordinary commercial metals, such as iron, zinc, lead, copper, tin, and antimony, may contain more or less arsenic as impurities. Further, commercial sulphuric acid is ordinarily made by the chamber process from sulphur derived from roasting iron pyrites, which usually contains arsenic, and, hence, some of this contaminating arsenic finds its way into the acid. As this acid is not infrequently used in the manufacture of hydrochloric acid from sodium chloride, this latter acid, also, becomes contaminated. It is clear, therefore, that there is a possibility of liberation of arsine whenever the contaminated acid acts upon such arsenic-containing metal. This toxic gas may, also, be liberated simply by the action of water upon the arsenides of the alkali metals.

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[1] See Gadamer, *Lehrbuch der chemischen Toxikologie,* 2te. Aufl., 1924, p. 49.

[2] See Bean, Amer. Gas. Assoc. Monthly, 1920, **2,** 265; or *Methods of the Chemists of the United States Steel Corporation for the Sampling and Analysis of Gases,* 3rd ed., 1927, p. 106.

Arsine is a colorless, inflammable gas, having a strong garlic-like odor. Its specific gravity is 2.695 as compared with air, one liter weighing 3.48 grams at 0°C. and 760 mm. pressure. The products of its combustion are arsenic trioxide and water. If the gas be passed through a tube, a portion of which is heated to redness, the gas is decomposed with the deposition of metallic arsenic on the cooler portion of the tube (this is the basis of the Marsh test discussed on page 512). Arsine burns with a blue flame, best seen when the gas emerges through a platinum tip and is ignited. A cold surface held *above* the flame is coated with a white crystalline deposit of the trioxide, while black arsenic stains will be deposited upon the cold surface, if this be introduced *directly into* the flame.

Arsine poisoning is always accidental,[1] and is caused by the inhalation of the gas generated along with hydrogen from materials containing arsenic as an impurity. As the contamination of the materials used in industrial processes is often unsuspected, cases of poisoning by arsine are often overlooked and attributed to other causes. "It is safe to say," says Hamilton,[2] "that in all instances of mysterious illness occurring among workers with metals or acids, a search for arsine fumes should be made."

Poisoning with arsine occurs, occasionally, with workers in chemical laboratories, Prof. Gehlen of Munich and Prof. Britton of Dublin having lost their lives from this cause. While not often reported, at least 10 cases are found in the literature of inhalation of this toxic gas during its preparation for demonstration purposes and in the course of medicolegal investigations in cases of arsenic poisoning.[3] Workers in aniline colors and those coming in contact with arsenical compounds in the laboratory may suffer with symptoms of arsine poisoning. Physicists and physiologists have in at least 5 cases been poisoned by inhalation of hydrogen arsenide in performing Tyndall's experiments of altering the timbre of the voice. Operatives in chemical industries, such as the manufacture of iron sulphate, zinc chloride and zinc sulphate, zinc smelting, roasting and extraction of mineral ores, manufacture of bleaching powder, etc., are subject to poisoning with arsine, Witthaus mentioning 38 cases of this type. Those engaged in filling toy ballons with hydrogen or in inflating or deflating war balloons have, not infrequently, suffered fatal poisoning from inhalation of this gas, Witthaus[1] collating 10 cases of the former type and 21 falling under the latter classification. Besides such cases as those cited above, poisoning with arsine may arise among workers employed in bronzing of brass, brazing, desilvering of lead by zinc, tinning of sheet iron, etc. Repairing or cleaning of tanks in which acids have been stored and cleaning out of the residue in Welden chlorine stills have resulted in poisoning from the fumes of hydrogen arsenide. Koelsch[2] has reported 11 cases occurring in the manufacture of V iron from arseniferous ore. Mild cases have been reported in the pickling rooms of steel mills, in which iron sheets are dipped into a bath of acid for a time, hydrogen being generated and carrying with it arsine, if either the acid or metal, or both, contain arsenic.[3] Jones[4] reports 5 cases among men engaged in the cyanide process for recovery of gold and silver. Hamilton[5] calls attention to several cases arising in the manufacture of coal-tar dye intermediates. Giordano[6] and Dudley[7] have reported a number of cases arising from arsine generated in the storage batteries of submarines. Ferro-silicon in the presence of moisture may give off arsine and phosphine, the former arising from the decomposition of the calcium arsenide contained in this material as an impurity. Several cases of this type of poisoning have been reported, especially among crews and passengers of ships carrying this substance.[8] A peculiar case of arsine poisoning is reported as arising from the possible electrolysis of water during a thunder storm and the formation of arsine by combination of the liberated hydrogen with arsenic in some copper dross, which a workman was putting into sacks.[9] From the above sources, as well as others not cited, 247 cases of hydrogen arsenide poisoning are found in the literature since 1815, of which 50 (20 per cent.) proved fatal.[10] The cases of poisoning from the liberation of a gaseous arsenical product from the pigments of wall paper, and formerly attributed to arsine, have been shown to be due to diethyl-arsine and not to arsine itself.[1]

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[1] The Boström case, reported by Becker (Diss. Giessen, 1888), may possibly be a case of suicide. See, Witthaus, *Toxicology*, 1911, p. 388.

[2] "Industrial Toxicology" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 783.

[3] See Witthaus, *Toxicology*, 1911, p. 389.

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[1] *Loc. cit.*, p. 390.

[2] Zentralbl. fur Gewerbehyg., 1920, **8**, 121.

[3] See Barker, St. Louis Med. & Surg. Jour., 1864, **1**, 29; Legge, House of Commons Rep., 1902, **12**, 234; Phelps, U. S. Naval Med. Bull., 1927, **25**, 754. In this connection see Muehlberger, Loevenhart and O'Malley, Jour. Ind. Hyg., 1928, **10**, 137, for a *suspected* case arising from this source.

[4] Jour. Amer. Med. Assoc., 1907, **48**, 1099.

[5] Jour. Ind. Hyg., 1921, **3**, 16. See, also, Wignall, Brit. Med. Jour., 1920, **1**, 826.

[6] U. S. Naval Med. Bull., 1917, **11**, 342.

[7] Jour. Ind. Hyg., 1919, **1**, 215.

[8] See Hamilton, Chem. Trade Jour., 1919, **65**, 365; and Glaister, *Medical Jurisprudence and Toxicology*, 4th ed., 1921, p. 724.

[9] See London Letter, Jour. Amer. Med. Assoc., 1923, **81**, 1537.

[10] See Muehlberger, Loevenhart and O'Malley, Jour. Ind. Hyg., 1928, **10**, 137, for a practically complete bibliography on the subject.

Symptoms.—Hydrogen arsenide is probably the most toxic of the inorganic compounds of arsenic. Although this gaseous arsenical is more rapidly and completely absorbed than those arsenicals introduced into the stomach, yet the symptoms do not usually appear for a few hours after exposure to the gas, while in poisoning with the ordinary inorganic arsenicals the symptoms usually appear within an hour or less. Further, the duration of a case of arsine poisoning is, as a rule, longer than one of common arsenical poisoning.

The symptoms in most cases begin with an indefinite feeling of faintness, giddiness and weakness, followed by intense headache, often chills, nausea and vomiting, and lumbar and epigastric pain. In some cases the vomiting may be an early symptom, and, in most severe cases, may become almost continuous, much as we observe it in other cases of arsenical poisoning. The specific action of the hydrogen arsenide appears to be exerted upon the hemoglobin of the red cells, marked hemolysis occurring and arsenic oxide being formed within the corpuscles. Labes[2] believes that the arsine is oxidized to a colloidal form of arsenic, which destroys the structure of the red cells. As a result of such action we find, as especial symptoms of arsine poisoning, hemoglobinuria, jaundice and lumbar pain, which are not noted in poisoning with the other inorganic arsenicals. In almost all cases pure hemoglobinuria may be observed, although at times methemoglobin,[3] hematin, and even blood itself may be found in the urine. The quantity of urine is usually normal, or even increased, at first, but later is diminished or even suppressed by the blocking of the renal tubules with the remains of the hemolyzed corpuscles. Jaundice is almost an unfailing symptom in arsine poisoning and develops to an extent commensurate with the severity of the poisoning. This jaundice is hepatogenous in origin, resulting from the formation of an excess of bile from the large amount of liberated hemoglobin.[4] In some cases this jaundice is evident in the yellowing of the conjunctivae and skin as early as the second day of the poisoning, while in other cases jaundice may be noted much earlier.[5] Lumbar pains occur early and are usually severe, although there are some cases in which they are not observed.

Besides the above manifestations of extensive destruction of the red cells, we note a relatively rapid anemia, which may be characterized by as low a red cell count as 868,000, although this is not usual except in the most severe cases.[1] Examination of stained slides of the blood show the red cells paler than normal, some of them punctated and some nucleated, while there was much cellular debris.

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[1] See page 482.

[2] Deutsche med. Wchnschr., 1926, 52, 2152 and 2192.

[3] See Mayer and Heubner, Biochem. Ztschr., 1929, **206**, 212.

[4] See Stadelmann, Arch. f. exp. Path. und Pharm., 1883, **16**, 221.

[5] See Trost, Vrtljschr. f. ger. Med., 1873, N. F., **18**, 269, in whose cases jaundice was noted by the workmen while they were at work.

If the subject survive the acute effects of arsine poisoning, symptoms more closely resembling those from arsenous oxide may develop. Arsine appears, according to Oettinger[2], to act on the central nervous system with the production of narcosis and paralysis, but he believes that it does not act on the peripheral nervous system. In the cases of Dudley[3], however, in which the arsine was developed from the battery plates of submarines, practically all the men exposed to the toxic gas showed signs of a mild neuritis, although this did not develop for some days, while Moresu[4] reports toxic neuritis with loss of function as a result of poisoning with arsine. While it is unquestionably true that polyneuritis is not usually a result of the action of arsine, yet the above cases indicate that it may occur in some cases. In the case of suspected arsine poisoning reported by Muehlberger, Loevenhart and O'Malley[5], the neuritis shown by the patient was of a severe and progressive type, but, although arsenical in type, was apparently due to ingestion of arsenic rather than to inhalation of arsine in the pickling room.

Although little is found in the literature that indicates that a true chronic type of arsine poisoning occurs, yet it would seem that such a possibility must be considered. Long-continued exposure to small amounts of arsine lead to vague symptoms, in which, as Henderson and Haggard suggest, the arsenic oxide liberated by the destruction of the red corpuscles may play a part in addition to the hemolytic activity of the gas itself. The cases of Dudley, cited above, probably are, in a sense at least, chronic in type, as the inhalation of arsine continued after symptoms started and, therefore, sufficient time was given "to superimpose the peripheral neuritis symptoms of chronic arsenic poisoning on the symptoms caused by the direct action of the gas on the blood." The diagnosis of the chronic type of hydrogen arsenide poisoning would rest to a certain extent on the finding of arsenic in the urine, but care must be taken that other sources of arsenic are excluded. Arsenic is rapidly excreted in the urine following arsine poisoning, as Wignall[6] has shown, but the complete elimination following an acute case may not take place for several weeks, Wignall indicating that, in 5 cases of acute arsine poisoning, the arsenic concentration of the urine fell from an average of 3.2 mg. As_2O_3 per liter immediately after the appearance of symptoms to a concentration of less than 0.1 mg. As_2O_3 per liter 34 days later. If the subject were inhaling daily small amounts of arsine, it is clear that his urine would show the arsenic for a considerable period of time after the exposure had ceased. In the case of suspected arsine poisoning discussed by Muehlenberger, Loevenhart and O'Malley[1], the urine of the subject was found to contain 0.77 mg. of arsenic 46 days after possible contact with arsine in the pickling room, an amount which was much too large for a chronic poisoning and was regarded as an indication that arsenic must have been taken by mouth after the subject had left his work. Guelman[2] has raised the question of chronic arsine poisoning when he says: "Does a form of chronic poisoning by arseniuretted hydrogen exist? This is the question that is confronting the Institute. Cases of acute poisoning are serious, but rare. Chronic poisoning, if it exists at all, does not manifest any acute specific phenomena, but, being repeated day after day, creates a chronic pathology, perverting the physiologic functions of the blood-generating system."

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[1] See Barié and Brissy, Bull. et mém. Soc. méd. des hôp. de Paris, 1904, 3s., **21**, 1059.

[2] Arch. f. exp. Path. und Pharm., 1917, **80**, 288.

[3] Jour. Ind. Hyg., 1919, **1**, 215.

[4] C. R. Soc. biol., 1918, **81**, 4.

[5] Jour. Ind. Hyg., 1928, **10**, 137.

[6] Brit. Med. Jour., 1920, **1**, 826.

Fatal Dose.—The exact amount of arsenic, in the form of arsine, which will cause death is difficult to state, owing to the fact that exact measurement of the fatal human dose is a difficult matter. It has been stated that the quantity inhaled by Gehlen (the chemist who met his death from arsine in 1815) could not have exceeded 1/100 grain, but this is uncertain. In the case reported by Schindler[3], the amount inhaled probably did not exceed 1/8 grain of arsenic. Dubitsky[4] states that several hours exposure to a concentration of 30 parts of arsine per million of air produces slight symptoms; Kohn Abrest[5] asserts that an exposure of 1 hour to a concentration of 50 parts per million is dangerous; while the U. S. Bureau of Mines[6] shows that an exposure of 30 minutes to a concentration of 250 parts per million is fatal to man.

Treatment.—The patient should be removed to the fresh air as rapidly as possible or given inhalations of oxygen. Later transfusion seems to be of some benefit in the acute cases. An attempt may be made to remove the arsine that has reached the blood and tissues by infusions of salt solution and the administration of mild alkaline drinks. The later treatment is symptomatic.

Postmortem Appearances.—The skin is dirty yellow in color and, on section, the internal organs show this evidence of jaundice. The mucous membrane of the stomach and small intestine are, likewise, slightly yellow in color and may show signs of inflammation. The liver may be normal in size and appearance or may be enlarged and show some fatty degeneration. The gall-bladder is usually enlarged and contains much bile. The spleen shows evidences of blood destruction in the deposits of blood pigment throughout the organ. The kidneys are congested and enlarged. The lungs may be edematous.

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[1] *Loc. cit.*

[2] Jour. Ind. Hyg., 1925, **7**, 6.

[3] Compt. rend. Acad. des Sc., 1890, **110**, 666.

[4] Quoted from Koelsch, Zentralbl. f. Gewerbehyg., 1920, **8**, 121.

[5] Ann. des Falsifications, 1915, **8**, 215.

[6] Technical Paper No. 248, 1921, p. 67. See Henderson and Haggard, *Noxious Gases*, 1927, p. 187.

Detection.—Arsine in the air may be detected by passing a large volume through a solution of cuprous chloride to remove hydrogen sulphide and phosphine and then passing a measured volume of this washed air over paper moistened with mercuric bromide solution (see Gutzeit Test, p. 515), and by comparison with standard bands the quantity may be determined.

It is probable that the isolation of arsine as such from the organs is not possible, as this gas is probably oxidized in the blood either to arsenic oxide or to some other form of arsenic. According to Sparth[1] arsine could not be isolated from organs by distillation *in vacuo.* On account of the change of the gas to some other combination of arsenic, the tests previously discussed serve for its detection and determination, so that the reader is referred to pages 506 *et seq.* for such methods.

HYDROGEN PHOSPHIDE

(Phosphuretted Hydrogen; Phosphine)

Three compounds of phosphorus with hydrogen are known, namely gaseous hydrogen phosphide (PH_3), liquid hydrogen phosphide (P_2H_4) and solid hydrogen phosphide (P_4H_2), the gaseous form being the only one of toxicological importance. Phosphine (PH_3) is readily prepared by boiling white phosphorus with potassium hydroxide solution, potassium hypophosphite and phosphine being formed by the reaction. This gas contains a little of the vapor of the liquid phosphine, so that it is spontaneously inflammable. Further, the impure gas is, also, formed by the action of water upon calcium phosphide, while the pure phosphine (which is not spontaneously inflammable) is produced by decomposing calcium phosphide with hydrochloric acid, or by the action of dilute acids upon metallic phosphides, such as those of zinc, iron, tin or magnesium. Calcium phosphide is, not infrequently, an impurity in calcium carbide, so that phosphine may be found as an impurity in acetylene to the extent of 0.04 to 0.06 per cent. Ferro-silicon is probably the source of most of the reported cases of phosphine poisoning, as this substance gives off, in the presence of moisture, a mixture of gases consisting of about 95 per cent. phosphine, 4 per cent. of arsine, and small quantities of acetylene and hydrogen silicide. According to Witthaus[2], one ton of ferrosilicon liberates 250 grams or 161 liters of hydrogen phosphide.

Hydrogen phosphide is a colorless gas, having a strong disagreeable odor much resembling that of decomposed fish. Its specific gravity is 1.185 as compared with air, one liter weighing 1.521 grams at 0° and 760 mm. pressure. While not spontaneously inflammable when in the pure state, it is, nevertheless, so inflammable that the heat evolved by the friction of the stopper on opening the bottle containing the gas may cause it to burn. It is slightly soluble in water, this solution decomposing in the light with the evolution of hydrogen and the separation of red phosphorus.

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[1] Chem. Zentralbl., 1918, **11**, 134.

[2] *Toxicology*, 1911, p. 680.

The literature contains reference to only a few fatal cases of poisoning with phosphine. Eulenberg[1] refers to the case of a man who inhaled quite a quantity of phosphine generated by the action of water upon calcium phosphide placed in a saucer outside the door of a room by a practical joker. Henderson and Clark[2] report the case of a young chemist who died from the effects of this gas with which he was experimenting. Other cases have been cited by Brenner[3] and by Bandler[4]. Most of the cases, however, have arisen from the production of phosphine by the action of moisture upon ferrosilicon, carried as a cargo in freight boats.[5]

Symptoms.—The action of phosphine seems to be exerted largely through the central nervous system, which it first slightly stimulates and then paralyzes. There is, apparently, no alteration in the blood, although it has been stated that there is some combination with hemoglobin. The symptoms, so far as they may be obtained from reported cases, are irritation in the throat, sensation of pressure in the chest, marked dyspnea, dry cough, dull headache, vertigo, roaring in the ears, purgation, general weakness, tremors, convulsions and death. Long continued exposure to the action of small amounts of phosphine seems to give rise to chronic symptoms somewhat resembling those of phosphorus poisoning.

Fatal Dose.—According to Henderson and Haggard[6] the maximum amount that can be inhaled for 1 hour without serious results is 100 to 200 parts per million of air; 400 to 600 parts per million are dangerous in 30 minutes to 1 hour; while 2000 parts per million prove rapidly fatal.

Postmortem Appearances.—The lungs may be hyperemic and edematous, with some areas of capillary hemorrhage; the liver and heart may be congested; the brain tissue shows, especially in animal experiments, some anemia, while the vessels of the meninges appear engorged with dark venous blood.

Detection.—Phosphine is detected by the method of Dusart and Blondlot, which is discussed in detail on page 400, to which the reader is referred.

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[1] *Lehre von der schädliche und giftige Gasen*, 1865, p. 437.

[2] Proc. Phil. Soc. of Glasgow, vol. 11, p. 517. Cited by Glaister, *Medical Jurisprudence and Toxicology*, 4th ed. 1921, p. 726.

[3] Sydenham Soc. Biennial Retrospect, 1865–66, p. 443.

[4] Prag. med. Wchnschr., 1879, **4**, 163.

[5] See Lehnkering, Ztschr. f. Unt. d. Nahr.- und Genussm., 1906, **12**, 132; Smith, Jour. Roy. Inst. Pub. Health., 1909, **17**, 1; Bruylants and Druyts, Bull. Acad. roy. de med. de Belg., 1909, 4s., **23**, 26; Robertson, Brit. Med. Jour., 1909, **1**, 1179; and Glaister, *Loc. cit.*, p. 724.

[6] *Noxious Gases*, 1927, p. 188.

NITROGEN DIOXIDE ("NITROUS FUMES")

There are three common oxides of nitrogen, namely, nitrous oxide (N_2O), nitric oxide (NO), and two forms of the dioxide (NO_2 and N_2O_4), the latter being often known as the tetroxide. Besides these oxides, which are relatively stable, there are two anyhdrides, nitrous anhydride (N_2O_3), which is almost entirely dissociated in the gaseous state into nitrous and nitric oxides, and the nitric anhydride (N_2O_5), which spontaneously decomposes into nitrogen dioxide and oxygen.

Nitrous oxide (*nitrogen monoxide, laughing gas*) is a colorless gas with a sweetish taste and smell. It has a specific gravity of 1.53, one liter weighing 1.97 grams at 0° and 760 mm. pressure. It is easily liquefied at 7°C. and 40 atmospheres pressure, in which form it is marketed in iron cylinders for use as an anesthetic. Nitrous oxide has no irritating effect, but produces, when in somewhat high concentration, anesthesia. Although nitrous oxide supports combustion, it can not support life, in consequence of which prolonged anesthesia must be carried out only when this gas is mixed with an atmosphere of approximately 20 per cent. oxygen. Inhalation of this gas has a tendency to induce laughing, from which characteristic it has been given the name "laughing gas". However, some individuals show rather a tendency to become sullen and pugnacious under its action. When properly used with oxygen the danger of using nitrous oxide for anesthesia is slight, but it must be stated that inhalation of this gas increases the blood pressure, so that with subjects with weakened vascular systems serious and, occasionally, fatal results, may occur. The death rate from its use seems to be about 1 in 100,000.

Nitric oxide (NO) is a colorless, irrespirable, highly toxic gas, which is very slightly soluble in water. It is probable that this oxide, although probably the most stable of the oxides of nitrogen, does not exist in atmospheric air, at least for any length of time, as it unites directly with oxygen in the cold to form the reddish-brown nitrogen dioxide (NO_2).

Nitrogen dioxide when hot is a deep brown, almost black colored gas, while when cold it is a pale yellow gas or a colorless liquid, which boils at 26°C. The density of the brown gas corresponds to the formula NO_2, while that of the yellow gas leads to the formula N_2O_4. The molecular form of this oxide is dependent, therefore, on the temperature of the gas. If the brown gas be heated above 156°C., the brown color begins to disappear, nitric oxide and oxygen being formed. This dioxide, in the form of NO_2, reacts with water and oxygen from the air to form nitric acid and nitric oxide, which latter is then oxidized and converted into nitric acid; while the dioxide, in the form of N_2O_4, reacts with water to form nitric and nitrous acids. "In whatever molecular form the dioxide is inhaled," say Henderson and Haggard[1], "it is at once altered to that corresponding to body temperature. At 40°C. approximately 30 per cent of the dioxide is in the form of NO_2 and 70 per cent as N_2O_4. It is in this proportion that the gases act upon the respiratory tract."

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[1] *Noxious Gases*, 1927, p. 134.

Nitrogen dioxide is evolved from the decomposition of nitric acid in the presence of heat, and, especially, in the presence of organic matter or metals. Thus, the spilling of nitric acid upon floors, or during storage or shipment, may lead to the liberation of sufficient nitrogen dioxide to produce serious results. In the manufacture of such explosives as guncotton, picric acid, trinitrotoluene, nitroglycerin, all of which are nitrated products, the liberation of "nitrous fumes" may be very extensive, the higher the nitration of the product the greater the danger from the fumes. So, also, when such modern explosives as ballistite, cordite, lyddite, and melinite, are employed in warfare, the gases of explosion contain a large percentage of nitrous fumes. The burning of celluloid, lacquer, artificial leather and photographic (movie) and *x*-ray films, liberates high concentrations of these nitrous fumes and has, on several occasions, lead to serious results. A somewhat less general hazard, but still one to be considered, is the liberation of fumes of the oxides of nitrogen in various chemical processes in the laboratory.

In 1911 Witthaus[1] collected 89 cases of poisoning by the inhalation of "nitrous fumes", of which 38 were fatal. In 1917 Hamilton[2], in a special study of the hazards in the manufacture of explosives, found 1389 cases of poisoning from inhalation of the oxides of nitrogen, 28 of which were fatal, the figures being regarded by her as not representing the actual number of cases in the ammunition plants, as many cases were probably not recognized by the physician. This large number of cases found during the period of the war was, no doubt, due to the high pressure under which such plants were working at the time, but it is probable that many cases will always be found in such plants even in times of peace.

Symptoms.—In cases of exposure to slight concentrations of the fumes, the subject "chokes up", the irritation causing a spasmodic contraction of the bronchi, such as takes place in bronchial asthma, and, often, there is a cramp-like pain in the abdomen, according to Hamilton. If the vapors are inhaled without admixture of air, there is a feeling of uneasiness and some loss of muscular power, accompanied by a sense of constriction in the chest, pain on inspiration, and some cough. The face may be pale, while the lips may show slight cyanosis. In the more serious cases, the onset is somewhat delayed, after the initial sense of slight suffocation. Owing to the insidious nature of these nitrous fumes, the one exposed may suffer little inconvenience at the time, but several hours later an intense dyspnea develops and death from pulmonary edema occurs shortly after. In Hamilton's cases, 16 of the 28 deaths were from this cause. Other cases, as mentioned by Hamilton, show an even more rapidly fatal course, the poison apparently acting on the nervous

[1] *Toxicology*, 1911, p. 301.

[2] Jour. Amer. Med. Assoc., 1917, 68, 1445.

centers, especially the respiratory center, the autopsy findings being comparatively insignificant[1]. In those cases which do not result fatally, recovery is slow and requires one or more weeks, in the course of which relapses showing many of the initial symptoms may occur[2]. In the recent disaster in the Cleveland Clinic, caused by the ignition and burning of x-ray films stored in the basement and the filling of the hospital with the mixed fumes of carbon monoxide, nitrous fumes, and, possibly, hydrocyanic acid gas, some 128 individuals were killed, many of them immediately, while others showed the somewhat characteristic delayed action of nitrous fumes. Muntwyler, Ray, Myers, and Sollmann[3] have reported the blood changes in some of these victims, showing that there was a concentration of the blood, with resulting increase of the hemoglobin values and the number of red cells, an increase of the pH and the carbon dioxide of the plasma, and a lowering of the chlorides.

Although workmen apparently become accustomed to these fumes to some extent, yet there is, probably, no immunity to their action. Constant breathing of the fumes probably produces some irritation of the throat and a chronic tracheitis, which may lead to a chronic cough. Hamilton, in her studies, was unable to find any evidence of chronic trouble from the inhalation of these fumes, but this may be due to the fact that the workmen do not stay long in any one part of the plant. Where small amounts of nitrous fumes are inhaled, it is to be expected that slight symptoms of the action of sodium nitrite may be noticed, owing to the fact that both nitric and nitrous acids are formed by the reaction of the nitrous fumes with the moisture of the respiratory tract, but such effects would not be noticed in the more intense irritation produced by the higher concentrations of the gas. According to Henderson and Haggard, "In men frequently exposed to low concentrations of nitrous fumes the rapidly acquired habituation to sodium nitrite prevents the development of systemic effects. Habituation in this respect does not, however, render the lungs less sensitive to irritation."

Fatal Dose.—The maximum concentration allowable for prolonged exposure is 39 parts of nitrogen dioxide per million of air; 117 to 154 parts per million are dangerous for even short exposure; while 240 to 775 parts per million are rapidily fatal for short exposure[4]. According to the Board of the Chemical Warfare Service appointed to investigate the Cleveland Disaster[5]," inhalation of 0.6 to 1 milligram per liter of air (0.029–0.049 per cent by volume, calculated as NO_2) quickly causes death. Inhalation of even smaller quantities may cause delayed death." In the Cleveland disaster some 128 persons lost their lives, some immediately, and others after a delayed period. In other cases death has been reported as occurring in from 5 hours to 40 hours.

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[1] See Hamilton, *Industrial Poisons in the United States*, 1925, p. 340.

[2] See Hall and Cooper, Jour. Amer. Med. Assoc., 1905, **45**, 396; Wood, Arch. Int. Med., 1912, **10**, 478.

[3] Jour. Amer. Med. Assoc., 1929, **93**, 512.

[4] See Lehmann and Hasegawa, Arch. f. Hyg., 1913, **77**, 323.

[5] Proceedings of a Board of the Chemical Warfare Service Appointed for the purpose of Investigating Conditions Incident to the Disaster at the Cleveland Hospital Clinic, Cleveland, Ohio on May 15, 1929, U. S. Gov't Printing Office, 1929.

Treatment.—The subject should be immediately removed from the contaminated air. If unconscious from carbon monoxide (in mixed gas poisoning) inhalation of oxygen, either pure or mixed with 5 per cent carbon dioxide should be resorted to at once. If respiration has ceased, artificial respiration should be practiced. The patient should be kept quiet and warm and closely watched for signs of beginning pulmonary edema. Early venesection is advisable. Intravenous injection of normal saline should be made as soon as evidence of edema appears. Drugs are, as a rule, contraindicated, as they are prone to overtax the weakened circulatory system, although where the heart shows signs of failure, stimulants may be necessary.

Postmortem Appearances.—The most marked changes are to be found in the thoracic organs. The mucous membrane of the larynx, trachea, and bronchi is reddened and hyperemic; the lungs are congested and edematous, the tissue appearing spleen-like on section, and showing crepitation only in a few places. The pleurae may be adherent over much of their extent. The cavities of the heart, especially those of the right side, may be distended with black tarry blood, which may be diminished in alkalinity or even slightly acid. The veins of the pia mater and the arteries at the base of the brain may be distended with dark blood.

Detection.—As the oxides of nitrogen form both nitric and nitrous acids on coming in contact with the moisture of the respiratory tract, these acids react with the alkali (especially the sodium) of the tissues, forming nitrates and nitrites. The detection of a case of poisoning from nitrous fumes would, probably, rest to a certain extent on the history of the case and the examination of the air to which the victim was exposed. The presence of nitric acid may be determined by the tests outlined on page 364. Nitrous acid may be detected by extracting the tissues with water, which will dissolve both the nitrites and nitrates formed. This extract may then be slightly acidulated with sulphuric acid and the liberated nitrous acid detected by the use of iodo-starch paper, a blue color appearing on the paper almost at once. Instead of using this method, one may employ the *Griess-Ilosvay test* as follows: Treat a few cc. of the extract with the reagent[1] and warm slightly, when a red color appears in the presence of nitrites. Moir[2] has introduced a very delicate test for nitrous acid or nitrites which is similar to the above, but seems somewhat easier from the quantitative side. Mix the liquid containing the suspected nitrite with from 1 to 10 cc. of solution A[1] and heat to 50°C. until complete diazotization takes place. Now add the same quantity of solution B[2] as was used of solution A. If nitrite is present an orange-red precipitate of p-nitrobenzeneazo-α-naphthol is formed quantitatively. Allow to stand for 1 hour and filter through a weighed Gooch crucible. Two hundred ninety-three parts of the precipitate is equivalent to 92 parts of NO_2 or 69 parts of $NaNO_2$. This dyestuff dissolves in sodium hydroxide solution with the formation of an intense blue-violet color, which may be used for colorimetric tests if desired.

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[1] Dissolve ½ gram of sulphanilic acid in 150 cc. of dilute acetic acid and add ⅒ gram of naphthylamine dissolved in 20 cc. of boiling water. On standing, a blue precipitate forms, which is separated and dissolved in 150 cc. of dilute acetic acid.

[2] Jour. South African Assoc. Anal. Chem., 1921, 4, 3.

WAR GASES

The employment of poisonous gases as a means of offensive warfare has made it necessary that physicians, many of whom will be called into service in times of war, should have some knowledge of the action of the various gases that may be met with and of the general lines of treatment which should be adopted to combat their effects. The use of gases in the World War proved so successful that it is highly probable that "Chemical Warfare" will play a very large role in future wars, should these occur.

As used in chemical warfare the term "gas" does not have any reference to the physical condition of the material when in the shells before being released. "It includes all materials that are carried to the enemy by the air after their escape from cylinders, bombs, shell or other containers. They may exist in the air in the form of true gases, smokes, finely pulverized solids, or even liquids." When the containers are broken open the liquids or solids are volatilized, either by the gas pressure or by the heat and force of the explosion. The effects produced by gases differ from those of other weapons of warfare, in that their action is distributed in reference to space and time to a tremendously greater extent than that of any other weapon employed. As pointed out by Brown,[3] "Gas differs in yet another way from any other weapon used in naval warfare in that the casualties produced differ according to the type of gaseous weapon used. When a bullet or shell is fired, its casualty-producing ability depends simply on whether or not a hit is made and the velocity and ballistic peculiarities of the missile. On the other hand, chemical warfare agents depend upon the physiologic effects which they produce for their tactical value. One group of agents may be primarily lethal, another may only produce temporary casualties of limited duration, another, prolonged casualties with little mortality, and still a fourth may be not toxic but only harassing by forcing wearing of the gas mask, thereby reducing efficiency to a serious extent." Besides this use of gases for offensive warfare, toxic gases may be met with during mining operations, or as the result of imperfect detonation or burning of explosives, so that the medical officer must be prepared not only to treat those exposed to the gases, but, also, to recognize the type of gas producing the effects.

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[1] Prepared by dissolving 1.5 grams of α-nitroaniline in 40 cc. of concentrated HCl and diluting to 500 cc.

[2] Prepared by dissolving 2 grams of ρ-naphthol, 1.1 grams of sodium hydroxide and 10 grams of sodium acetate in 500 cc. of water.

[3] United States Naval Med. Bull., 1928, **26,** 217.

According to Brown[1], the chemical warfare agents which are standard at the present time may be classified as follows:

		Chemical Warfare Service Symbol	*Common Name*	*Chemical Name*
1. Physical (ordinary state temperatures).....	(*a*) Gases.	Cl.	Chlorine	Chlorine.
		CG	Phosgene	Carbonyl chloride
	(*b*) Liquids.	HS	Mustard	Dichlorethylsulphide.
		Ml	Lewisite	Chlorvinyldichlorarsine.
		PS	Chlorpicrin	Trichlornitromethane.
		CA	Brombenzylcyanide	Same.
		CC	Crude Oil	Mixture.
		FM	Titanium tetrachloride	Same
	(*c*) Solids.	DA	Diphenylchlorarsine	Same
		DM	Diphenylaminechlorarsine	Same
		CN	Chloracetophenone	Same
		HC	Hexachlorethane	Same
		P	Phosphorus	Same

2. Tactical Use...
   - (*a*) Lethal agents: Cl, CG, PS.
   - (*b*) Severe direct casualty agents: HS, Ml, CG, Cl, PS, WP.
   - (*c*) Temporary casualty agents: DA, DM.
   - (*d*) Harassing agents: CN, CA.
   - (*e*) Screening agents: WP, FM, HC, CC.
3. Physiological effects........
   - (*a*) Lung irritants: Cl, CG, PS.
   - (*b*) Vesicants: HS, Ml.
   - (*c*) Lachrymators: CA, CN.
   - (*d*) Sensory irritants: DA, DM.
   - (*e*) Screening smokes: HC, P, FM, CC.
4. Persistency[1]....
   - (*a*) Persistent chemical agents: HS, Ml, CA.
   - (*b*) Semipersistent: PS.
   - (*c*) Nonpersistent: All others.

[1] An agent is persistent, if 10 minutes after its release in the open, under conditions which are favorable for the use of the chemical, there is sufficient remaining at the point of release to require protection for personnel.

For our purposes the poisonous gases of most importance are the lung irritants and the vesicants, although the lachrymators, sensory irritants and screening smokes cause temporary injury and incapacitate the men exposed to them to such an extent that they become ineffective military agents.

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[1] *Loc. cit.*

PHOSGENE

Phosgene ($COCl_2$, *carbon oxychloride, carbonyl chloride*) is the most irritant of the group of lung irritants. At ordinary temperatures it is a gas possessing a peculiar, very unpleasant, pungent odor, and having a specific gravity of 3.46. It can be condensed at a low temperature to a colorless liquid which boils at 8°C. and which has a specific gravity of 1.432 at 0°C. The compound is readily decomposed by water into HCl and CO_2. Phosgene is prepared in several ways, the simplest method, probably, being the treatment of equal volumes of chlorine and carbon monoxide in the direct sunlight. The decomposition of chloroform and carbon tetrachloride by heat often leads to contamination of the air in laboratories and industrial plants. Chloroform spontaneously oxidizes to phosgene when it is exposed to light in the presence of air, so that chloroform which is to be used for anesthesia must be carefully protected against such possible change. Carbon tetrachloride is widely used, at the present time, in the form of "pyrene" in fire extinguishers, and as "carbona" as a noninflammable cleansing agent, so that the possibility of the formation of phosgene from such agents must be borne in mind. During the World War many cases of poisoning arose from the use of phosgene, while an extensive accidental "mass poisoning" of 300 individuals in Hamburg with 10 deaths is reported by Hegler.[1]

Symptoms.—In some points phosgene holds an intermediate position between chlorine and nitrous fumes. Though it is a more intense eye irritant than chlorine, it is not so immediately irritant to the upper respiratory passages, so that there is a definite delay in the development of poisoning by phosgene. Symptoms may be delayed for a number of hours, so that gassed subjects may go about for some time with only slight discomfort and then become rapidly and seriously poisoned. Chlorine attacks vigorously the moist mucous membrane lining the upper portions of the respiratory tract, but phosgene seems to exert its effects more upon the smaller bronchioles and alveoli, owing, possibly, to the fact that the hydrolysis of this gas under the influence of moisture takes place very gradually, which fact may account for the delay in the appearance of the symptoms. While the irritant action of phosgene is supposed to arise from the HCl liberated, yet it would appear that phosgene is much more toxic than the equivalent concentration of free HCl.[2]

The first symptoms noted are smarting and watering of the eyes, irritation and burning in the nose, throat and trachea, coughing, dyspnea, and a sensation of tightness and constriction of the chest. All of these signs of sensory irritation of the respiratory passages *may* appear immediately on exposure, but an insidious onset is, probably, more common. In those heavily gassed, nausea, retching, and vomiting may be prominent features. The symptoms with the higher concentrations are proportionately more violent and, probably, more rapid in appearing. The symptoms of respiratory embarassment become more marked, the breathing becoming spasmodic, rapid and shallow, the pain in the chest more marked, headache may be marked, and there is often extreme restlessness and mild delirium, although some cases may show a semi-comatose condition. In most cases, the signs of pulmonary edema appear in a few hours, the symptoms of asphyxia and anoxemia becoming prominent. In these cases two groups of symptoms may be observed. In the first group, we find marked venous engorgement (*blue stage asphyxia*). "The ears, lips, and, progressively, the entire face assume a cyanotic, bluish-red tint which may deepen to the intense violet of advanced cyanosis, and there may be visible distention of the superficial veins of the face, neck, or chest. There are copious frothy sputum, frequent cough, with respirations of 40 to 48 per minute, elevated temperature, and a full, strong pulse in the neighborhood of 100. This condition is most frequently seen on the second day after gassing." The second group comprise those suffering from circulatory collapse (*gray stage asphyxia*). "The patient may recover from blue stage asphyxia or he may pass into the gray stage as the result of a dilated and failing heart. The color becomes an ashen gray, the expression anxious and staring, and respiratory difficulty is shown by the strained effect of the muscles around the nostrils. There is intense oxygen want. The breathing is markedly hurried and shallow and a rapid running pulse of 130 or over develops. The prognosis is distinctly bad in this stage and the outcome is usually determined within 72 hours of the time the victim was gassed. Apparent recovery from gray stage asphyxia may be succeeded by a severe or even fatal broncho-pneumonia."[1]

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[1] Deutsche med. Wchnschr., 1928, **54,** 1551.

[2] See *Noxious Gases* by Henderson and Haggard, 1927, p. 137. Also, Rona, Ztschr. f. d. ges. exp. Med., 1921, **13,** 16.

Fatal Dose and Fatal Period.—Phosgene is ten times as toxic as chlorine, producing toxic effects in concentrations of 0.3 ounce per 1000 cubic feet (0.3 mg. per liter) after an exposure of 30 minutes. The maximum concentration allowable for prolonged exposure is 1 part of phosgene per million of air; 25 parts are dangerous for even short exposure, and over 25 parts are rapidly fatal.[2]

"Four-fifths of the deaths occur", say Smith and Lucke, "in the first twenty-four hours, very few succumb after the third day. Sometimes a man who at first seemed to be slightly gassed may toward the end of the first day become gravely ill, and die; but from the end of the second day onward there is no danger to be apprehended with the less grave cases. Broncho-pneumonia not infrequently develops, and is responsible for the occasional deaths that occur later than the end of the first week. As a rule, the patient recovers readily after the third day, but though he may soon be out of immediate danger, complete recovery of cases of even moderate severity may take a considerable time." One of the cases of Hegler[1] died in 4½ hours, while another lingered for 11½ days.

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[1] Brown, U. S. Naval Med. Bull., 1928, **26**, 217. See, also, Flury, Ztschr. f. d. ges. exp. Med., 1921, **13**, 1; Laquer and Magnus, Ibid., 31 and 200; Heitzmann, Ibid., 180; "Death from Asphyxia" by Smith and Lucke in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 396; Gilchrist, Mil. Surg., 1924, **55**, 247; Ibid., 1928, **63**, 477.

[2] See Henderson and Haggard, *Noxious Gases*, 1927, p. 137.

Treatment.—Rest is the most important measure in the handling of "gassing". Victims should not be allowed to move about, and must be prevented from undergoing any physical strain, in order to reduce the respiratory requirements and prevent any strain upon the weakened heart. As far as possible such patients should be kept in a recumbent position and in the fresh air. Warmth is needed in many of the severe cases, especially at the outset when they are collapsed and the skin is cold. If the patient is out of doors, special care should be taken to protect him against chill, as this might lead to a subsequent broncho-pneumonia. Oxygen should be administered on the first sign of cyanosis and should be continuous, and given in high concentration, but not under too high pressure, owing to the possibility of rupturing the damaged lung tissue, about 6 liters per minute being sufficient in the average case. To relieve the edema and assist the circulation, venesection should be resorted to early, and as much as 400 to 600 cc. should be withdrawn at one time. Gilchrist[2] states, however, that bleeding should never be resorted to in the gray pallid cases with a weak and rapid pulse. Special stimulants and drugs do not seem to be of much value.

Postmortem Appearances.—When death occurs in the late part of the first day, the trachea may be moderately congested, and the smaller bronchioles may show a somewhat greater degree of congestion. The lungs are usually large, heavy, edematous, and dusky red. The cut section drips frothy blood. Patches of emphysema alternate with areas of collapse, and, occasionally, interstitial emphysema may be found extending to the mediastinum. The pleural cavities usually contain clear or blood-stained fluid. The heart may be dilated, or normal in size. In those dying on the fourth day or later, broncho-pneumonia or pleurisy are usually present. The blood is more concentrated than usual, shows a high red count along with high hemoglobin values, although, in some cases at least, a marked conversion of hemoglobin to hematin obtains.[3] Thrombosis may develop and punctate hemorrhages may be found in some of the organs, especially the brain, and marked degenerative changes of the nerve substance may obtain.[4] The kidneys may be enlarged and congested.

CHLORPICRIN

Chlorpicrin (CCl_3NO_2, nitrochloroform, trichlornitromethane) is a liquid at ordinary temperatures and pressures, boiling at 112°C. Its tendency to evaporate is approximately that of water. It is a rather stable compound and does not decompose readily. It is, however, so toxic that concentrations of vapor such as will rise from this liquid are still strong enough to have undesirable physiological action.[1]

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[1] Deutsche med. Wchnschr., 1928, **54,** 1551.

[2] The Mil. Surg., 1928, **63,** 477.

[3] Mayer, Deutsche med. Wchnschr., 1928, **54,** 1557.

[4] Wohlwill, Ibid., 1553.

The principle action of chlorpicrin appears to take place in the medium sized and smaller bronchi. It, therefore, occupies a position intermediate between chlorine and phosgene. In the lower concentrations its action is such as to produce vomiting; at higher concentrations or if inhaled for long periods at lower concentrations, it is a lung irritant. Besides these actions it is a lachrymator, being, in reality, the first one of this group to be used in the World War. "The use of this agent in surprise shoots on enemy troops not well trained and so unable to get into their gas masks promptly results in their becoming victims of the vomiting action of this agent; while they are thus engaged a lung irritant will be received by them generally, will be much more effective, as they are unmasked." The symptoms of poisoning by chlorpicrin are much the same as those of chlorine and phosgene, pulmonary edema being the effect of its irritant action on the lungs. The toxicity of chlorpicrin is manifested in a concentration of 0.8 ounces per 1000 cubic feet of air, and is, thus, approximately 4 times as toxic as chlorine and ⅓ as toxic as phosgene, providing the exposure lasts for ½ hour.

MUSTARD GAS

This substance was first used in the World War in 1917 at Ypres and has been called, therefore, *Yperite*. Chemically this compound is thiodiglycolchloride, or $\beta\beta'$-dichlorethylsulphide $(CH_2ClCH_2)_2S$. It is a heavy oily liquid at ordinary temperatures and pressures, becoming a solid at 14°C. and boiling at 214°C. Its specific gravity at 20°C. is 1.274. When pure it is practically colorless, but may have a light straw, pink, or even brown color. It has a faint odor, resembling that of water cress and suggestive of sulphur compounds. As Wood[2] points out, this odor is so slight as to be of no value as a warning against its presence, especially as the olfactory nerve is quickly exhausted on exposure to small concentrations of the gas. The liquid is almost insoluble in water, slightly soluble in paraffin or vaselin, and practically soluble in alcohol and other organic solvents, vegetable oils and fats. The liquid vaporizes very slowly at ordinary temperatures and is very slowly decomposed by alkaline solutions, but is readily destroyed by dry chloride of lime. The peculiarity of this compound in volatilizing and recondensing with variations in temperature makes it one of the most "persistent" substances used in the War. This compound must not be confused with the real oil of mustard, allyl isothicyanate, $CH_3CH:CHSCN$.

Symptoms.—"On exposure nothing is noticed at first save the faint, though characteristic smell of the gas. After the lapse of two or three hours the eyes begin to smart and to water, and the conjunctivae soon become reddened. The nose begins to run with thin mucus, as from a severe cold; sneezing is frequent. Nausea, retching, and vomiting occur at frequent intervals during the next few hours. The conjunctival irritation increases in intensity, the throat feels dry and burns; the voice becomes hoarse, and a dry cough develops. The skin becomes dusky, and reddened, and especially on the face and the neck the affected areas look as if they had been scorched, but they are almost painless; other portions of the body become similarly affected. This is followed by the development of small blisters in the involved areas. At the end of twenty-four hours a typical appearance is presented. The patient lies virtually blinded, with tears oozing between bulging eyelids over his reddened and blistered face; there is a constant nasal discharge and an occasional harsh, hoarse cough. Respiration is fairly normal; there may be frontal headache and marked photophobia. Death practically never occurs during the first twenty-four hours. During the second day the condition is aggravated by the development of large blisters over the reddened areas, while the external genitalia become edematous and painful. Severe tracheitis and bronchitis are present, with abundant expectoration of muco-pus, sometimes containing actual sloughs from the inflamed mucosa. The temperature, pulse-rate, and respiratory rate are increased. Secondary infection of the necrotic mucous membrane soon leads to the development of bronchopneumonia, which frequently terminates fatally."[1] Various functional disturbances, as well as certain pathologic changes, such as peribronchial thickenings, have been attributed to the late effects of gassing, but Koontz[2] shows that there is little or no pathologic basis for the symptoms noted by the soldier, and in later work[3] has demonstrated that gassing with mustard gas has, in reality an inhibitory effect on the development of pulmonary tuberculosis, especially in animals.

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[1] See Wood, The Mil. Surg., 1928, **62**, 322.

[2] *Loc. cit.*

Fatal Dose.—This is a difficult matter to determine. The degree of injury produced by "mustard" is proportional to the concentration of the gas, time of exposure to it, individual susceptibility, moisture, etc. At its smallest concentration it is a lachrymator. At slightly higher concentrations it is a lung irritant, Wood[4] stating that respiration of a concentration as small as 0.001 mg. per liter for about 1 hour would result in the production of lung lesions in human beings. According to Brown[5] mustard is nearly 50 times as toxic as chlorine and 4 to 5 times as toxic as phosgene, 0.07 ounce per 1000 cubic feet producing toxic effects after an exposure of 30 minutes. Mustard is a very powerful vesicant, so much so that persons exposed to its vapors almost invariably become casualties, but fatal results practically never arise from this action.

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[1] See "Death from Asphyxia" by Smith and Lucke in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 398.

[2] Arch. Int. Med., 1925, **36**, 204.

[3] Koontz, Ibid., 1927, **39**, 833; Ibid., 1929, **43**, 90.

[4] The Mil. Surg., 1928, **62**, 322.

[5] U. S. Naval Med. Bull., 1928, **26**, 217.

Postmortem Appearances.—In the mildest cases a superficial degeneration and necrosis of the epithelium of the mucous membrane of the respiratory tract obtains, along with congestion and some edema. In more severe lesions a deeper necrosis of the respiratory mucosa is noted, with the formation of a diphtheritic[1] membrane in the anterior nares, pharynx, larynx, and upper portions of the trachea. The lungs are slightly enlarged, but they do not show the marked edema so characteristic of the action of phosgene. There is extreme pulmonary passive congestion, the tissue feeling doughy without any elasticity. The alveolar capillaries are markedly engorged. There may be found, in cases of early death, areas of emphysema alternating with collapsed portions, and patches of petechial hemorrhage. Large portions or even whole lobes may become hepatized.[2] The other internal organs show nothing characteristic. On the skin may be observed areas of irritation varying from simple erythema to the most intense vesication.

Treatment.—Remove the patient to fresh air as quickly as possible. Change the clothing promptly to prevent further exposure from contamination through the clothing or equipment of the soldier. Give patient a shower bath with hot water and soap, providing this can be done within 30 minutes after the exposure. Bathe the eyes either with a boric acid lotion or with a solution of bicarbonate of sodium, 30 parts per 1000. The liquid mustard may be removed from the skin by sponging with such solvents as kerosene, carbon tetrachloride or alcohol. This procedure may have to be repeated several times if the mustard has been in contact with the skin for any length of time. For the burns of the skin, employ sponging with bicarbonate solution and the application of a dressing of boric acid and calcium hypochlorite, or use impervious dressings such as paraffin sprays, olive oil or vaselin. The treatment of the pulmonary symptoms should be the same as that outlined for phosgene.

LEWISITE

This compound is chlorvinyldichlorarsine ($ClCH{:}CHAsCl_2$). This compound is of doubtful value as a war gas, when in its gaseous phase, as it is rapidly hydrolyzed by the moisture in the air. However, when it comes in contact with the subject, it is a powerful vesicant and produces violent irritation to the respiratory mucous membranes on inhalation. These effects differ from those of "mustard" in being much more prompt, the respiratory irritation following almost immediately on exposure. The vesication is marked, so that Lewisite may have the still further effect of inducing arsenical poisoning from absorption of the compound through the abraded area. These special arsenical symptoms are marked hemolysis of the red cells leading to hemoglobinuria, the development of anemia and jaundice, and, later, peripheral neuritis. It is estimated, according to Brown, that the application of 0.02 cc. of Lewisite per square centimeter per kilo of body weight is a fatal dose for a man. Lewisite is somewhat more toxic than is "mustard", 0.05 ounce per 1000 cubic feet of air being toxic after a 30 minute exposure.

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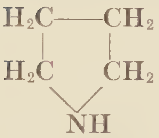
[1] See Warthin and Weller, Jour. Lab. and Clin. Med., 1917, **3,** 447; Ibid., 1918, **4,** 229.

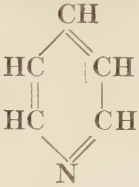
[2] See Winternitz, Mil. Surg., 1919, **44,** 476; also, Covey and Barron, Amer. Jour. Med. Sci., 1919, **157,** 808.

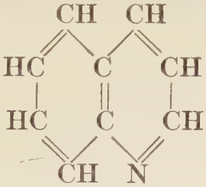
CHAPTER XXI

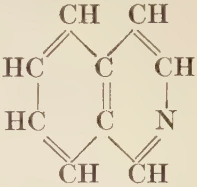
ALKALOIDAL POISONS

An all-embracing and unobjectionable definition of an alkaloid is very difficult to formulate. They have been defined as the basic substances found in plants, but this definition is too broad. The tendency at the present time is to regard as alkaloids those nitrogen-containing plant products, which have the nitrogen bound in cyclic combination as a derivative of pyrrolidine, pyridine, quinoline, or isoquinoline. While this conception covers, for the most part, the substances known as alkaloids, yet it is faulty (1) in that at least one alkaloid, narceine, has the nitrogen in an aliphatic chain attached to a benzene ring, and (2) as it assumes that all alkaloids have only one nitrogen in the ring compound, whereas pilocarpine has two nitrogen atoms in the glyoxaline ring. It must be understood, further, that the constitution of some of our most important alkaloids has not been definitely determined as yet, so that the above tentative definition may have to be considerably modified later.


Pyrrolidine.


Pyridine.


Quinoline.


Isoquinoline.

There are many basic substances found in the higher fungi as well as in the animal body, these latter compounds being known as leucomaines, while the bacterial decomposition of vegetable or animal protein leads to the formation of the so-called putrefactive bases or ptomaines. These compounds are, for the most part, nitrogen bases of open chain carbon atoms, although some agree with the simple closed chain structures of the pyridine type, and others have the nitrogen in closed chains of other than the six-membered rings, indol, for instance, being of the type of a pyrrol ring joined to a benzene nucleus. The so-called alkaloids of tea and other beverage plants are derivatives of purin ($C_5H_4N_4$), in which class belongs, also, the uric acid group of leucomaines.

The alkaloids are the chief poisonous principles of plants, and appear to be quite widely spread in the plant kingdom, although they are very unequally divided among the different classes and families of plants. Most of the alkaloid-bearing plants belong to the Dicotyledones, only the *Colchicaceae*, among the Monocotyledones, producing alkaloids, while none of the Cryptogamia contain these basic bodies. The *Papaveraceae*, *Solanaceae*, *Ranunculaceae*, and *Rubiaceae* are especially rich in alkaloids. Plants, which belong to the same family, usually contain the same or similar alkaloids, while the same alkaloid is rarely found in different families. It should be stated, also, that the same plant may contain several alkaloids.[1] These basic bodies are not distributed in equal amounts in the different parts of the plants, so that the official preparations are made from those portions which are the richest in alkaloid content. It is rare that the alkaloids are found in the plant in the free condition, but exist, rather, in the form of salts bound to certain acids present in the specific plant.

Properties.—With respect to their physical state alkaloids may be divided into two groups: (1) Non-volatile alkaloids, which are very numerous, are composed of carbon, hydrogen, nitrogen, and oxygen, are usually colorless or white crystalline solids, melting when heated and usually subliming with partial decomposition, but are odorless and incapable of distillation unchanged; and (2) the volatile alkaloids, comparatively few in number, composed of carbon, hydrogen, and nitrogen, without oxygen, for the most part liquid when free as bases, and are markedly odorous and capable of distillation unchanged.

Both classes of alkaloids are capable of neutralizing ordinary acids, without the liberation of hydrogen or formation of water, with the formation of salts, thus corresponding to ammonia in its production of ammonium salts. The free bases and the alkaloidal salts differ in their solubilities in different menstrua. Thus, the free alkaloids are, for the most part, either insoluble or difficultly soluble in water, but more or less readily soluble in alcohol, ether, chloroform, benzol, amyl alcohol, or other immiscible solvents; while their salts, for the most part, are soluble in water or alcohol, especially in the presence of free acid, but are with few exceptions insoluble in the immiscible solvents mentioned. It should be remembered, however, that the differences in solubility of the alkaloids and their salts in the menstrua above mentioned are relative and not absolute, and that traces of the free alkaloids may dissolve in water, for instance, while traces of the salts may dissolve in the immiscible solvents, so that one may lose a large part, or even all, of these alkaloids in his extraction processes if great care is not taken. Upon these differences in solubility of the bases and their salts, however, are based the methods of extracting the alkaloids from the complex mixtures in which they may exist.[2] Most of the alkaloids are precipitated from aqueous solutions of their salts by the addition of caustic alkalies, although such precipitates may be dissolved in some cases (especially atropine, cocaine, and morphine) by an excess.

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[1] See Schmidt, "Alkaloide" in *Handbuch der biologischen Arbeitsmethoden*, edited by Abderhalden, 1920, Abt. 1, Teil 9, S. 49. For discussions relative to the production of alkaloids in plants see Pictet, Arch. der Pharm., 1906, **244**, 389; Ber. d. d. chem. Ges., 1907, **49**, 3771; Annett, Biochem. Jour., 1920, **14**, 618; Thatcher, *The Chemistry of Plant Life*, New York, 1921.

[2] See page 344 *et seq.*

General Alkaloidal Precipitants.—There are a large number of reagents for the precipitation of alkaloids as a group, inorganic combinations, such as double salts and perhalides, and a few organic combinations, all insoluble in water, being thrown down rather promptly on adding these reagents to aqueous solutions of the alkaloidal salts.[1] It is to be said, however, that many of these reagents also precipitate proteins and their derivatives, so that the purification processes outlined on page 346 must be carefully performed before one is in a position to draw conclusions as to the actual presence of an alkaloid. Care must be taken not to use too much of the extracted material in these tests, as in so doing the possibility may arise of not having sufficient for the more specific tests to be outlined under each alkaloid. The method recommended by Gadamer[2] is a very efficient and reliable one for the detection of an alkaloid. A small portion of the dried residue, obtained in the extraction processes, is treated with a single drop of dilute (1:50) sulphuric acid and slightly warmed to bring it into solution. By means of a fine-pointed glass rod transfer a portion of this solution to a small watch glass resting upon a black background, and then add a small drop of the reagent. If an alkaloid be present, a precipitate will be observed at the point of contact of the two liquids, or even throughout the mixture. These precipitates may be either amorphous or crystalline, depending upon the special alkaloid in question, and are of the nature of difficultly soluble salts. Many alkaloidal precipitants have been advocated, but we shall limit ourselves to a discussion only of those that appear to us most serviceable and reliable, cautioning the worker not to attempt to use all of these general reagents for fear of using up too much of his valuable material. We believe that the best results may be obtained by working with one each of the different types of these reagents, and, therefore, recommend the tannic acid, the phosphomolybdic, and either the Mayer's or Dragendorff's tests.

Owing to the possible presence of extractive material, other than alkaloids, in the matter to be tested, care must be taken in interpreting the results obtained with these general reagents. Under the action of many of these precipitants a slight turbidity is generally obtained, due possibly to leucomaines or ptomaines, so that such a slight turbidity may, as a rule, be accepted as either a negative result for poisonous alkaloids or, at least, the presence of too small an amount to be precipitated. A definite precipitation with a general reagent, applied to a well purified extract of the tissues, certainly calls for the application of special tests for the specific alkaloids. "A considerable precipitate by a general reagent cannot be taken as conclusive of the presence of a vegetable alkaloid, still less of a poisonous one."

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[1] Much of the material in this section is taken from the article on "Alkaloidal Poisons" by Prescott and Webster in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 416.

[2] *Lehrbuch der chemischen Toxikologie*, 2te. Aufl., 1924, S. 479.

1. *Iodine in Potassium Iodide Solution* (*Wagner's Reagent*).—This is a decinormal solution of iodine in potassium iodide solution, containing 12.692 grams of purified iodine and 18 grams of potassium iodide dissolved in 1 liter of distilled water. This reagent is added in excess to an acidulated, but not to an alcoholic, solution of the alkaloid. The precipitates, of varying shades of dark brown to black color, are periodides, and are usually flocculent and amorphous, but may become crystalline. The free alkaloid may be recovered from these haloid precipitates by dissolving them in sodium thiosulphate solution, alkalinizing with sodium hydroxide, and shaking out with the proper immiscible solvent.

2. *Potassium Mercuric Iodide Solution* (*Mayer's Reagent*).—This is a N/20 solution, containing 6.788 grams of mercuric chloride and 25 grams of potassium iodide dissolved in a liter of distilled water. The reagent should always be applied in an acidulous solution, and in the absence of alcohol or acetic acid. The precipitates are yellowish-white in color, and are crystalline or become so on standing. The free alkaloid is obtained by treating the precipitate with stannous chloride solution, alkalinizing with sodium hydroxide solution, and extracting with an immiscible solvent.

3. *Potassium Bismuth Iodide Solution* (*Dragendorff's Reagent*).—This solution is prepared by dissolving 80 grams of bismuth subnitrate in 200 cc. of concentrated nitric acid and 272 grams of potassium iodide in 250 cc. of water, adding the bismuth solution to the iodide solution slowly and with constant stirring, allowing to stand for 24 hours, filtering, and making up to 1 liter.[1] Espinos[2] recommends that this reagent be prepared by saturating a 10 per cent solution of potassium iodide with bismuth iodide. This reagent is applied to acidulated solutions of alkaloids in the absence of ether and amyl alcohol, and produces orange-red precipitates, which are often crystalline.

4. *Phosphomolybdic Acid* (*De Vry's or Sonnenschein's Reagent*).—This reagent is prepared as follows: Dissolve 150 grams of crystallized ammonium molybdate in 1 liter of distilled water, and pour this solution into 1 liter of concentrated nitric acid. To this mixture add a warm solution of disodium hydrogen phosphate until no further precipitation of ammonium-phospho-molybdate occurs. Filter off the yellow precipitate, wash it with water, and dissolve it in a hot solution of sodium carbonate. Evaporate this solution to dryness and ignite at a low red heat until all ammonium salts are volatilized. Moisten the residue with nitric acid and ignite once more. This product, which is sodium phosphomolybdate, is now dissolved in 10 times its weight of a mixture of 1 volume of concentrated nitric acid and 9 volumes of distilled water. This reagent is a close precipitant of the alkaloids, forming yellowish, usually amorphous

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[1] See Cappelli, Ann. chim. applic., 1924, **14,** 261; Abs. in Chem. Abs., 1925, **19,** 223.

[2] Ann. méd. lég. et de criminol et police sci., 1927, **7,** 213.

precipitates with most alkaloids, although some may become crystalline on standing. If these precipitates be mixed with sodium carbonate, the free alkaloid is liberated and may be extracted with immiscible solvents.

5. *Tannic Acid.*—This acid is used as a freshly prepared 5 per cent. aqueous solution, and gives white, grayish, or yellowish precipitates with most alkaloids. In most cases, however, the precipitates are soluble in acids, even in excess of the reagent, so that care must be taken to apply this test to simple aqueous solutions of the alkaloidal salts and, also, not to use an excess of reagent.

Color Tests.—Besides the above-mentioned reagents, which act as group precipitants, there are many substances or mixtures which form with the alkaloids, as well as with certain glucosides, organic synthetic compounds, or even protein derivatives, changes of color which may be, in some cases at least, more or less characteristic. It is to be said, however, that the alkaloidal residue to be tested by such reagents should be as nearly pure as possible, as some impurities in themselves give color changes which may obscure those of the alkaloid; others may produce similar colorations; while still others may prevent the formation of the coloration with the alkaloid.

While, possibly, no single reaction is to be regarded as sufficient to warrant a conclusion as to the absolute identity of a certain residue, yet it may lead to the application of other color tests, which, collectively, are conclusive. Although some of these color tests yield somewhat similar results with different alkaloids, careful comparison will usually reveal slight variations which assume importance in toxicological work. The variations may be either in the initial color, the final color, or in the sequence of colors noted, so that the play of colors in the reaction must be carefully noted. Certain of these reagents react with so many of the alkaloids, even though the colorations noted may be varied, that they may be regarded as general reagents; while others often yield such a definite and characteristic color, or play of colors, that they are, more especially, classed as special reagents.

A single color test is rarely, if ever, to be regarded as conclusive as to the absolute identity of a residue, owing to possible influences of impurities. "It should be insisted upon, where possible, that all of the more important and well-established reactions shown by the pure alkaloid be obtained with the purified residue extracted from the tissues, if one is to give an unequivocal opinion as to identity." Such a rigid requirement cannot always be fulfilled, owing to the small amount of material isolated, so that, in such cases, the analyst should be somewhat guarded in his deductions. The method of making these color tests is the following: Place a small amount of the solid residue on a porcelain testing plate or in a flat porcelain dish and, by means of a fine-pointed glass rod, apply a drop of the reagent. Excess of the reagent, as well as of the residue, is to be avoided, as the most characteristic results are obtained with small quantities, and, further, as the amount of material available is limited.

The reaction should be watched closely, the initial color, the sequence of colors, and the final color being noted, as each of these points may determine the identity of the residue.

The color reactions of alkaloids may be classified, according to Henry[1], as (1) those produced by dehydrating agents, such as concentrated sulphuric acid; (2) those given by oxidizing agents not of themselves yielding colors, such as nitric acid, chlorine, or sulphuric acid mixed with such oxidizing agents as potassium dichromate, manganese oxide, lead oxide, ceresoceric oxide; (3) those yielded by oxidizing agents which themselves give a colored product by reduction, such as iodic acid, and reagents containing chromic, molybdic, tungstic, arsenic, selenic, and vanadic acids; (4) colorations produced by special reagents, such as ferric chloride. Perhaps, the general reagents best suited for preliminary or "orientation" tests for the alkaloids are concentrated sulphuric acid, nitric acid, and Fröhde's reagent, although others might be used. Many other reagents have been advocated, but most of these are, in reality, special in character, so that they will be taken up under the specific alkaloid with which they are especially associated.

1. *Concentrated Sulphuric Acid.—No color*, or only a faint straw shade, is given by pure aconitine (which is rarely obtained), atropine, cocaine, codeine, scopolamine, hyoscyamine, gelsemine (occasionally shows a yellow followed by brown), morphine (often light red if reagent is impure), nicotine, quinine, quinidine, and strychnine.

Yellow, orange, or brown colorations are given by berberine, colchicine, delphinine, and lobeline. *Yellow tints followed by red or violet* are noted especially with the alkaloids of veratrum.

Red, purple, or violet colors are yielded by impure aconitine, apomorphine, brucine (due to impurity of nitric acid in the reagent), impure cocaine, coniine, impure gelsemine, narcotine, and physostigmine.

2. *Concentrated Nitric Acid.—No coloration* is noted with pure aconitine, atropine, cinchonine, coniine, gelsemine (may show yellow or green if impure), quinine, and strychnine.

Yellow tints are obtained with impure aconitine, berberine, codeine, gelsemine, morphine (may show red), narcotine, and veratrine.

Red, purple or violet colors are given by impure aconitine, apomorphine, berberine, brucine (deep red), and physostigmine.

3. *Fröhde's Reagent.*—This is prepared by dissolving 1 or 2 mg. of molybdic acid in 1 cc. of chemically pure sulphuric acid, although some specify higher proportions of molybdic acid, but these appear to lessen the distinctiveness of the test. As this reagent is gradually reduced on standing, it must be freshly prepared just before use. This reagent gives colorations with many alkaloids, but its most distinctive reaction is, probably, with morphine.[2]

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[1] Allen's Commercial Organic Analysis, 4th ed. 1912, **6**, 198.

[2] There are many other reagents, which give special colors with certain alkaloids, and which consist of solutions of reducible compounds in sulphuric acid. Among these we

No color is produced with atropine, cinchonine, coniine, hyoscyamine, nicotine, scopolamine, and strychnine. *Yellowish colorations* are observed with aconitine and colchicine. *Reddish shades* are noted with brucine and veratrine. *Bluish colors* are given by codeine and morphine (purple fading to violet, then dirty green, yellow, and finally to faint pink). *Greenish shades* are yielded by apomorphine, berberine, and quinine.

Biologic Tests.—Biologic or physiologic tests are those used to detect poisons by studying their action upon living plants or animals, which serve as living reagents.[1] These methods may be employed both for qualitative and quantitative determination, the poison being usually administered in aqueous or very slightly acidulated (acetic acid) solution. The animals most frequently used are frogs and white mice, although rabbits and guinea-pigs, not infrequently, yield more characteristic results, while the human subject may serve better in detecting the physiologic properties of such alkaloids as aconitine and atrophine. The intensity and rapidity of the observed action will depend upon (1) the amount of the poison employed; (2) the method of application; (3) upon the size and weight of the animal employed; and (4) upon the type of animal used. "Each test, chemical or biologic, is to be valued upon its merits, judged from all known data in the experience of chemists, pharmacologists, and practical analysts." These biologic tests will be discussed in detail under the alkaloids to which they are especially applicable.

It is to be remembered that the delicacy of the tests for alkaloids as a class, as well as for specific members of the group, is not exceeded by the delicacy of the tests for inorganic poisons. The reactions for alkaloids are, as a rule, so sensitive that very small amounts, indeed, are necessary for their identification, but such tests can be applied only when the alkaloid has been isolated from the large mass of other organic material present. For this reason, the excretion of alkaloids from the tissues must be very carefully performed, all precautions being taken to guard against possible loss. Failure to observe this condition of analysis may result in complete failure to isolate and identify an alkaloid which is, in reality, accountable for the death in question. As Prescott has so well said, "There is 'analytic error' even in inorganic analyses, and when dealing with colloidal matter in masses, several tens of thousands times larger than the crystalloid poisons to be recovered, the unavoidable 'analytic error' may exceed the ratio of the quantity of the poison, or leave less than what is needful for identification." The separation of the alkaloids from the tissues is, therefore, a task far more delicate than the extraction

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find Erdmann's Reagent (a sulphuric acid containing a very small amount of nitric acid), Rosenthaler and Türk's Reagent (an arsenic-containing sulphuric acid), Selmi's Reagent (a saturated solution of iodic acid in sulphuric acid), Brociner's Reagents (solutions of ammonium niobate, potassium ruthenate, ammonium uranate, or ammonium tellurate in conc. H_2SO_4), Mandelin's Reagent (ammonium vanadate in conc. H_2SO_4), Mecke's and Lafon's Reagents (solutions of selenic acid in conc. H_2SO_4) and Luchini's Reagent (solution of potassium dichromate in conc. sulphuric acid).

[1] See Fühner, *Nachweis und Bestimmung von Giften auf biologischen Wege.* Berlin, 1922.

Alkaloid.	Mayer's reagent.	De Vry's reagent.	Concentrated sulphuric acid.	Concentrated nitric acid.	Concentrated sulphuric acid with oxidizing agents as potassium bichromate, manganese dioxide, lead oxide.	Fröhde's reagent.	Specially valuable tests for identification.
Aconitine.	Yellowish-white non-crystalline precipitate.	Yellowish-white precipitate.	No color when pure. Yellow to red when impure.	No color when pure. Yellowish or red when impure.	Slight yellow colorations, becoming light green on standing.	Yellowish or orange.	Crystalline form, m.p. and percentage of gold in chloraurate Biologic test.
Atropine.	Yellowish-white crystalline precipitate.	Yellowish; turns blue with NH_3.	No color.	No color.	Lemon yellow changing to green.	No color.	Character of the precipitate with gold chloride. Vitali's test. Biologic tests.
Cocaine.	Yellowish-white crystalline precipitate.	Yellowish-white precipitate.	No color when pure. Reddish if impure.	No color.	Light yellow, changing to orange and finally green.	No color. Slightly yellowish on standing.	Character of double chlorides of gold and platinum. Seiter's test. Biologic tests.
Codeine.	Yellowish-white crystalline precipitate.	Brownish-yellow precipitate.	No color at first. Becomes blue on long standing.	Yellowish in cold. Reddish if heated.	Light yellow, changing to brown and finally greenish.	Yellowish, deep green, finally blue.	Ferric chloride, Mecke's tests and Tunmann's tests.
Colchicine.	No precipitate in dilute solutions. Yellowish-white in concentrated.	Yellowish-white precipitate.	Lemon yellow color. Violet if acid is impure.	Violet red, changing to green and then to yellow.	Light yellow, showing greenish streaks as oxidizing agent is drawn through. Becomes dark yellow and then light yellow.	Yellow solution, changing to yellowish-green and back to yellow.	Nitric acid and ferric chloride tests. Barillot's test. Biologic test with mice.
Gelsemine.	Yellowish-white crystalline precipitate.	Yellowish-white precipitate.	No color when pure. If impure, yellow followed by brown.	No color if pure. May show yellow or green if impure.	Reddish purple or cherry red without initial blue or violet. Liquid assumes green or bluish-green tint.	Purple or reddish-violet.	Concentrated sulphuric acid with oxidizing agents. Biologic tests.
Morphine.	Yellowish-white crystalline precipitate.	Yellowish-white precipitate.	No color when pure. May get light red due to nitric acid in reagent.	Orange. May show slight reddish tone.	Green.	Purple, fading to violet, then dirty green, yellow, and finally pink.	Fröhde's, Marquis', Husemann's, Lefort's, and Pellagrini's test.
Physostigmine.	Yellowish-white crystalline precipitate.	Yellow amorphous precipitate.	No color.	No color or slight reddish yellow.	Light yellow with faint greenish tint.	Slightly reddish-yellow.	Rubreserin test. Ammonia test. Da Silva's test.
Strychnine.	Yellowish-white crystalline precipitate.	Yellowish-white precipitate.	No color.	No color.	Blue to purple, then violet, reddish, rose-pink, finally yellow.	No color.	Bitter taste. Fading purple test. Crystalline test. Biologic test.
Veratrine.	Yellowish crystalline precipitate.	Yellowish-white precipitate.	Yellow; soon orange, green fluorescence, red, carmine red.	Yellowish, changing to red.	Lemon yellow, changing to brownish-red, then deep brown.	Yellow, changing to reddish.	Sulphuric acid test. Sulphuric acid and cane-sugar test. Biologic test.

of inorganic poisons. The detailed methods of extraction have been previously discussed on page 344, to which the reader is referred. Certain variations from this procedure will be given in special cases, in which modifications are necessary.

Precipitation of Alkaloids with Lloyd's Reagent.—Instead of following the general methods of extraction of alkaloids as outlined previously, Lloyd's reagent may often be advantageously employed to precipitate these basic bodies, thus obviating many difficulties that arise in the other methods and minimizing the possibility of saponification. This reagent[1] is a highly hydrated aluminum silicate in colloidal form, and is derived from fuller's earth, although Lloyd's Canadian patent (203,257, August 24, 1920) calls for the use of hydrous magnesium silicate.

This reagent is employed as follows: Extract the finely hashed tissue with acidulated water or alcohol, as in the usual processes, employing low temperatures when the easily saponifiable alkaloids are suspected. Filter the acidified extract, and wash the residue thoroughly. Add to this clear filtrate 1 or 2 grams of finely powdered fuller's earth made into a thick paste with a little water. Shake thoroughly and allow the earth to settle out. Filter, collecting the entire sediment on a small filter, washing with water until there is no reaction for the acid originally in the solution. Allow the residue to dry slightly, and transfer it to a separatory funnel; add a little water, alkalinize with ammonia water, and shake out with the proper immiscible solvent. Withdraw the solvent, and re-extract two or three times. Now evaporate the combined solvents to obtain the alkaloid, which is, usually, amorphous, but may become crystalline, and is quite pure. There may be some question whether the recovery is actually quantitative by this method, as the earth holds the absorbed alkaloid with great avidity[2], but, it is to be remembered that the usual processes of extraction are not without inherent error.

Quantitative Determination of Alkaloids.—It is evident, from what we have previously said, that the estimation of the absolute amount of alkaloid in the tissues examined in any given case is, at best, only an approximate one. If the final residue be not sufficiently purified, a positive error arises; while a very decided minus error may arise in the efforts to obtain a perfectly pure alkaloid. The analyst should report his results as so much alkaloid actually recovered, and never state that the amount reported represents the exact quantity present in the tissues. It is not always possible to obtain quantitative values for the alkaloids, owing to the very small amount sometimes isolated, but, in every case of forensic importance, some statement regarding quantities isolated must be given.

The most satisfactory method is, probably, the ordinary gravimetric one, which consists in actually weighing the amount of pure alkaloid isolated from a given quantity of tissue. Knowing the weight of the entire organ, it is a matter of a simple calculation to determine the total amount of alkaloid in the organ, assuming, of course, that the alkaloid is equally and uniformly distributed throughout the organ.

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[1] See Lloyd's Letters Patent, No. 1,048,712, December 31, 1912. See, also, Lloyd, Amer. Jour. Pharm., 1916, **88**, 217; and Waldbott, Jour. Amer. Chem. Soc., 1913, **35**, 837.

[2] See Gordin and Kaplan, Amer. Jour. Pharm., 1914, **86**, 461; and, also, Clowes and Walters, Jour. Amer. Med. Assoc., 1920, **75**, 655.

As a check upon this gravimetric determination, the residue after weighing may be dissolved or softened by the addition of about 1 cc. of neutral alcohol or ether, and a volumetric estimation of the alkaloid made. Add a known volume of N/100 sulphuric acid and a little water to the dissolved alkaloidal residue, warm slightly to insure complete solution of the alkaloid, and titrate the excess of acid present, using N/100 sodium hydroxide solution as the neutralizing agent, and cochineal, methyl-red, or iodeosin as an indicator. Subtract the amount of alkali solution added to produce neutrality from the amount of N/100 acid originally employed to obtain the amount of acid combined with the alkaloid. Each cc. of the N/100 acid thus combined represents $^{1}/_{100000}$ of the molecular weight of the alkaloid to be determined expressed in grams.

Identification in Analysis.—As has been previously mentioned, bacterial decomposition of the tissue proteins leads to the formation of the so-called ptomaines (cadaveric alkaloids or putrefactive bases). In times passed, and even to some extent at present, these bodies occasionally become confused with the true alkaloids, which may be the cause of a homicidal poisoning. Although greater numbers of such putrefactive bases are becoming known, and as a result the danger of mistaking these ptomaines for true alkaloids might seem to be greater, yet it must be realized that our knowledge and resources of analysis are, also, increasing, so that we are in a much better position to avoid the pitfalls before us. "All vegetable alkaloids, with a few exceptions, can be characterized as such by their chemical and physiologic behavior, so as to be recognized in the presence of ptomaines. A careful and experienced worker of today will not confound a vegetable alkaloid with a ptomaine that is known and worked out, since, in spite of the great number of ptomaines, none has been observed to give reactions uniform in all points with any plant base." The worker should attempt to purify his residues as much as possible, and should, then, investigate these by chemical, physical, and biological methods, remembering that differences will be shown between ptomaines and true alkaloids in some of the reactions. Exceptions to these general statements may, perhaps, be made in cases of poisoning by muscarine, and certain actively poisonous bases of the pyridine and hydropyridine series, as the last-named bases occur, also, among the products of putrefaction. In such cases the proof of the occurrence of a true poisoning from analytic results alone is not only very difficult, but, in the majority of cases, impossible.

VOLATILE ALKALOIDS

This group comprises very few members. These alkaloids contain carbon, hydrogen, and nitrogen, but no oxygen, and are, for the most part, liquid when free as bases, are possessed of marked and somewhat characteristic odors, are strongly alkaline in reaction, and are capable of distillation unchanged. These basic compounds are rarely used in medicine, with the possible exception of sparteine, and have highly toxic properties.

CONIINE

This alkaloid is found in *Conium maculatum* (common or spotted, "poison" hemlock), along with 5 other alkaloids, methylconiine, conhydrine, pseudoconhydrine, γ-coniceine, and ethylpiperidine. Coniine is found in all parts of the plant, being especially prevalent in the seeds, and is the characteristic poisonous alkaloid of conium, although γ-coniceine is from 15 to 18 times more toxic than is coniine, while the other alkaloids show reactions similar to those of coniine, but much weaker. The toxic properties of conium were known to the ancients, who used it as a judicial poison, Socrates, among others, having been put to death

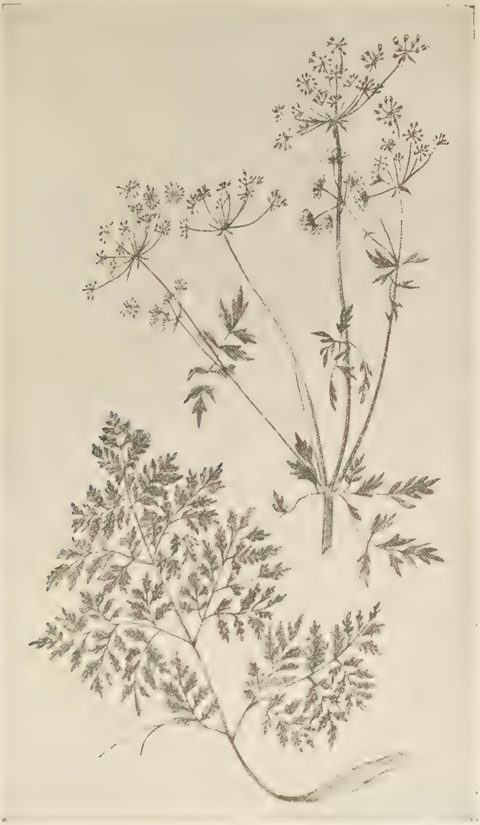
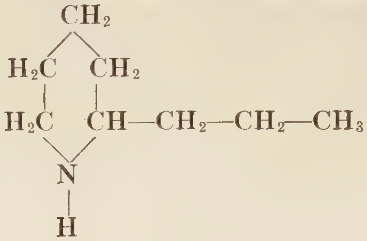


FIG. 48.—Hemlock (Conium maculatum). (Prescott and Webster in Peterson, Haines and Webster, "Legal Medicine and Toxicology".)

by drinking its infusion.[1] It has been used in producing homicidal[2] and suicidal death,[3] while several accidental cases have occurred from eating the root in mistake for horse-radish or parsnips, or the leaves instead of parsley[4], or from mixing hemlock seeds with anise seeds.[5] According to Witthaus[6] only 6 cases, 3 of them fatal, have been caused by overdoses of either the tincture or fluid extract of conium.

Properties.—d-Coniine ($C_8H_{17}N$) was first isolated by Giesecke[7] and was the first alkaloid to be synthesized.[8] In his later work Ladenburg[9] showed that synthetic coniine was really isoconiine, which could be converted into d-coniine by heating to 300°C. Structurally speaking, d-coniine is the simplest of the alkaloids, being known chemically as α-n-propyl-piperidine and graphically represented as follows:



d-Coniine, when pure, is a colorless, almost odorless, dextrorotatory, oily fluid, but soon becomes yellow and, after long standing, resinous, and acquires a peculiar, penetrating, characteristic odor described as "mousy", this odor being especially noticeable when coniine is diluted with water. It is strongly alkaline in reaction, and neutralizes acids perfectly. It is somewhat volatile at ordinary temperatures and distills with alcohol or water, being found in the distillate from alkaline solutions in the systematic process for poisons. At higher temperatures it distills unchanged in an atmosphere of hydrogen, but undergoes slight decomposition in presence of air. It boils at approximately 166°C. Its specific gravity at 20°C. is 0.844, while its specific rotation at 19°C. is $[\alpha]_D = +15.7°$. In the cold d-coniine solidifies to a crystalline mass, which becomes fluid at -2°C. It is soluble in 90 parts of water, less soluble in hot water, the cold saturated solution becoming turbid on heating. It is readily soluble in alcohol, ether, ethyl acetate, chloroform, petroleum ether, benzol, and acetone, being easily removed from aqueous or alkaline solutions by these immiscible solvents, and, to a slight extent, from slightly acid solutions by ether. This alkaloid readily forms salts, which are colorless and odorless, and are soluble in water, alcohol, and chloroform, but not in petroleum ether. On adding a fixed alkali to these salts the peculiar "mousy" odor is developed. For the properties of the other alkaloids of conium see Prescott and Webster[1].

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[1] See Imbert-Gourbeyre, *De la Mort de Socrate,* Paris, 1875; Lewin, *Die Gifte in der Weltgeschichte,* Berlin, 1920, p. 67.

[2] See Mitscherlich and Casper, Vrtljschr. f. ger. Med., 1859, **15,** 193; Hofmann, Ibid., 1870, N. F., **13,** 1; Taylor, *On Poisons,* 3rd Amer. Ed., 1875, p. 700; Kunkel, *Handbuch der Toxikologie,* 1900, **2,** 658.

[3] See Schauenstein in Maschka's *Handbuch der gerichtlichen Med.,* 1881, **2,** 573.

[4] See Med. Times and Gaz., 1855, **2,** 51 for report of 50 deaths from this cause: also Bennett, Edin. Med. and Surg. Jour., 1845, **64,** 169.

[5] See Galtier, *Traité de toxicologie médicale,* 1855, **2,** 206.

[6] *Toxicology,* 1911, p. 922.

[7] Arch. der Pharm., 1827, **20,** 97.

[8] Ladenburg, Ber. d. d. chem. Ges., 1884, **17,** 772, 1121, and 1676; 1885, **18,** 47, 913, 1587, and 2961; 1886, **19,** 2578.

[9] Ibid., 1906, **39,** 2486.

Symptoms.—These vary somewhat, depending, possibly, on the amount of γ-coniceine present. If the free alkaloid be taken, there is a burning sensation in the mouth and throat. The general symptoms are languor and drowsiness, which does not pass into actual sleep, prickling sensations in the muscles, muscular weakness, pain in the head, twitching and tremors together with stiffness and rigidity of some of the muscles, apparently arising from a partial paralysis of the peripheral nerves.[2] The movements are weak and unsteady, the gait being staggering. Nausea and, occasionally, vomiting with profuse salivation occur. Speech is thick. Deglutition is difficult. Heart is at first slowed, but later accelerated. Respiration at first accelerated and deepened, later becomes slow and labored, weak and irregular, and finally ceases. In most cases there is little disturbance of the intellect, although dulling of the special senses may be noted. The pupils are somewhat dilated as respiratory failure proceeds, the failure of this function being the cause of death, the terminal asphyxia probably being due to paralysis of the nerve terminations in the respiratory muscles, rather than to depression of the respiratory center, although the latter may be accountable for cases of rapid death.[3]

Fatal Dose.—The minimum lethal dose of pure coniine is uncertain. In the experiments by Schroff[4] upon 27 physicians, 3 to 85 mg. dissolved in alcohol produced toxic effects; while Tiryakin[5] was able gradually to increase the dose to 150 mg. without causing much discomfort. Kobert states that 130 mg. is the lowest fatal dose, and that from 30 to 60 mg. is a seriously poisonous quantity. In the case of Louise Berger, poisoned by her lover Dr. Jahn, death resulted from a dose of 10 to 15 drops (420 to 630 mg.). As 1 drop of coniine weighs about 42 mg., it is clear that 1 to 2 drops would be a distinctly poisonous dose.

Fatal Period.—The poisonous effect of coniine is very rapid, fatal results being usually reached in ½ to 3 hours, Louise Berger dying in a few minutes.[6] So far as the literature reveals only 3 cases of a longer duration than 3 hours are known; the case of Bennett[1] in which death occurred in 3½ hours; that of Pepper[2] in 7 hours; and that of Armstrong[3] in 52 hours.

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[1] "Alkaloidal Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 488.

[2] See *A Text-Book of Pharmacology and Therapeutics* by Cushny, 9th ed., revised by Edmunds and Gunn, 1928, p. 323.

[3] See *Toxikologie* by Starkenstein, Rost, and Pohl, 1929, p. 440.

[4] Wchnbl. d. k. k. Gesellsch. der Aerzte in Wien, 1856, **2**, 33, 49, 73, and 102. Cited by Witthaus, *Toxicology*, 1911, p. 923.

[5] *Étude experimentelle et clinique sur la conine et ses sels,* Thèse de Paris, 1878.

[6] See Arch. der Pharm., 1861, **47**, 257 and 360.

Treatment.—Evacuation and lavage of the stomach with solution of tannin, and stimulating agents and measures, with every effort, including artificial respiration, to maintain the respiration, constitute the treatment. Coniine is excreted rapidly in the urine, so that the effects pass off fairly soon if death does not result.

Postmortem Appearances.—These are not especially characteristic, being largely those due to asphyxia. The brain and its meninges show congestion, while the lungs are congested and, occasionally, edematous. The blood is dark and fluid. If the pure alkaloid is taken, the mucous membrane of the esophagus and stomach may show considerable hyperemia, with some ecchymotic areas, owing to the corrosive character of the alkaloid.

Detection.—Coniine may be found in most of the internal organs in cases of poisoning, while the stomach contents and urine may be especially rich in their alkaloidal content. In the systematic examination of the tissues for poisons, coniine will be found in the distillate from alkaline solutions, when searching for volatile poisons as discussed on page 338; or may be obtained in the process for alkaloids, according to Haines' modification of the Dragendorff method as outlined on page 344, in the petroleum ether extraction of the alkaline solution.

If the method for volatile poisons be employed, the odor of the distillate may furnish a clue to the presence of coniine. Neutralize the distillate from the alkaline solution with oxalic acid, and evaporate this mixture to dryness. Extract the residue with alcohol, which dissolves the coniine oxalate, leaving behind any ammonium oxalate present. Filter and evaporate to dryness. On now adding a little caustic alkali to this residue, the free coniine is liberated and may be recognized by its odor. Extraction of the alkalinized residue with petroleum ether will furnish the pure alkaloid on evaporation of the solvent, just as is the case with the residue obtained when the systematic process for alkaloids is used. This alkaloidal residue may be identified by the following tests.

1. *General Properties.*—These have been discussed in some detail on page 612. Although the odors of coniine and nicotine are very distinct and characteristic, yet some workers have an impaired sense of smell, so that reliance can not always be placed on this property to distinguish between these alkaloids, which are obtained at the same points in the general processes. Coniine is alkaline to litmus and phenolphthalein, differing from nicotine in the fact that its alcoholic solution reddens an alcoholic solution of this latter indicator, while an

[1] Edinb. Med. and Surg. Jour., 1845, **64**, 169.

[2] Med.-Leg. Jour., 1885–86, **3**, 179.

[3] Trans. Med. Soc. New Jersey, 1880, **114**, 249.

alcoholic solution of nicotine does not. With aqueous solutions of both coniine and nicotine, phenolphthalein gives a red color, which disappears on shaking with chloroform in the case of nicotine, but is permanent with coniine. Chlorine water renders an aqueous solution of coniine turbid, while it has no effect on solutions of nicotine. Bromine water produces a crystalline precipitate with coniine and not with nicotine. According to Autenrieth[1] the general alkaloidal reagents especially sensitive to coniine are iodo-potassium iodide (1:8000), phosphomolybdic acid (1:5000), potassium mercuric iodide (1:8000), and potassium bismuthous iodide (1:5000). Gold and platinum chlorides fail to precipitate coniine when the concentration is less than 1:100, whereas they precipitate nicotine when the concentration is as low as 1:5000.

2. *Crystallization Test.*—The vapor of coniine with that of hydrochloric acid produces a white cloud in the air. If a watch-glass be moistened with free coniine, another watch-glass moistened with HCl, and the latter glass fitted over the former, the upper glass will receive a deposit of white crystalline, doubly-refracting needles arranged in stellate groups or in dendritic forms, or, later, cubical or octahedral crystals of coniine hydrochloride.

3. *Oxidation Reactions.*—Pure coniine is not colored by concentrated sulphuric or nitric acids. With concentrated sulphuric acid and oxidizing agents, such as vanadic acid, potassium bichromate, selenic acid, and potassium permanganate, greenish colors are obtained, which change into brown or red on standing or heating.[2] If coniine be present in sufficient amount, warming of the alkaloid with dilute sulphuric acid and potassium bichromate yields butyric acid, which may be recognized by its odor.

4. *Melzer-Dilling Reactions.*—To 0.5 cc. of a fairly strong alcoholic solution of coniine add a few drops of carbon disulphide, boil and add excess of water. On now adding a few drops of copper sulphate solution a brown color is produced, which is taken up by ether and yields, on evaporation of the solvent, flat, brown, rhomboid plates. Piperidine gives positive results with this test, but nicotine does not.

If uranium nitrate be added instead of copper sulphate in the test above, and the solution shaken with toluol, this solvent becomes red in the presence of coniine. Nicotine does not yield this reaction.[3]

5. *Biologic Test.*—If from 5 to 10 mg. of coniine hydrochloride be injected into the lymph-sac of a frog, the animal lies on its back and completely loses its reflexes in 15 minutes. If the ischiatic nerve be exposed within 1 to 2 hours after the injection, no contraction of the foot is seen in electric stimulation, although the muscle itself responds promptly. If at least 15 mg. of coniine hydrochloride be injected subcutaneously into a frog, typical paralysis of the extremities will be observed, the animal becoming

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[1] *Detection of Poisons*, 6th Amer. Ed., translated by Warren, 1928, p. 155.

[2] See Dilling, Pharm. Jour. 1909, 4 ser., **29**, 34, 70 and 102.

[3] See Melzer, Ztschr. f. anal. Chem., 1898, **37**, 352 and 357; Ibid., 1902, **41**, 327; Dilling, *Loc. cit.*, p. 103.

limp and dragging the legs when moving (curare-like action). Neither nicotine nor the coniine-like ptomaines exhibit this reaction.[1]

Coniine-like Ptomaines.—In the examination of cadaveric material for the presence of coniine, it must be remembered that volatile, alkaline, liquid, putrefactive substances, either of endogenous or exogenous origin, may be found, which may simulate coniine to a certain extent. Most of these liquid putrefactive bases have been identified as monamines or as diamines, some of the latter, such as cadaverine and putrescine, although open-chain compounds, being derivatives of piperidine. As these products, as well as derivatives of pyridine, are found in putrefying material, it follows that the positive identification of coniine is extremely difficult and often impossible in the presence of a large amount of decomposing animal tissue. Although the chemical reactions for coniine are not distinctive, many of them being given by piperidine itself, the biologic tests are not shown by any "cadaveric coniines" yet isolated. However, these physiologic tests require more material than is always at the disposal of the worker. Confusion[2] has occurred in the past in medicolegal cases, but differentiation is possible if the work be carefully done. A positive statement that coniine is actually present must be guardedly made. The analyst should insist that the symptomatology and postmortem findings be consistent with coniine poisoning and that the biologic tests be positive, the identity of the chemical reactions being further confirmation.

NICOTINE

Nicotine ($C_{10}H_{14}N_2$) is the only constituent of tobacco (*Nicotiana tabacum*) which possesses any toxicologic interest, although at least three other alkaloids, nicoteine ($C_{10}H_{12}N_2$), nicotimine ($C_{10}H_{14}N_2$), and nicotelline ($C_{10}H_8N_2$), have been isolated from tobacco by Pictet and Rotschy[3], while Noga[4] reports the finding of 4 alkaloids besides nicotine, to which he gives the names, nicotoine ($C_8H_{11}N$), nicoteine ($C_{10}H_{12}N_2$), isonicoteine ($C_{10}H_{12}N_2$), and nicotelline ($C_{10}H_8N_2$).

Nicotine exists in all parts of the tobacco plant[5], but especially in the leaves, which contain from 0.6 to 8 per cent, depending upon the kind of tobacco, in combination with malic and citric acids. Pipe tobacco contains from 0.518 to 0.854 per cent. while cigars yield 0.801 to 2.887 per cent., the finer grades showing less nicotine than the ordinary grades,[6] and cigarettes have a nicotine content running from 1.06 to 2.89 per cent, the so-called "denicotinized" brands showing, in reality, but little less nicotine than the ordinary varieties.[1]

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[1] See Kobert, *Lehrbuch der Intoxikationen*, 2te. Aufl., 1906, **2**, 1081; and Fühner, *Nachweis und Bestimmung von Giften auf biologischem Wege*, Berlin, 1911, 87 and 111.

[2] In this connection see Otto, *Anleitung zur Ausmittelung der Gifte*, 6te. Aufl., 1892, p. 93; Brouardel and Boutmy, Ann. d'Hyg., 1880, 3 S., **4**, 352; Selmi, *Sulle Ptomaine*, 1878, p. 22.

[3] Ber. d. d. chem. Gesellsch., 1901, **34**, 696.

[4] Cited by Schmidt, "Alkaloide" in Abderhalden's *Handbuch der biologischen Arbeitsmethoden*, Abt. 1, Teil 9, 1920, p. 129.

[5] Starkenstein, Rost, and Pohl, *Toxikologie*, 1929, p. 426, state that nicotine is probably found, also, in *Cannabis indica* and in the leaves of *Duboisia Hopwoodii*.

[6] Schmidt, *Loc. cit.*, p. 130. See, also, Brooke, Philipp. Jour. Sci., 1925, **26**, 497.

Tobacco is used very widely in the form of pipe tobacco, cigars, cigarettes, and chewing tobacco. To a less extent it is employed as a snuff, which is made from the so-called "snuff leaf" and from refuse tobacco. Commercial nicotine is used rather extensively as a germicide and insecticide, the strength of such solutions varying from 30 (or lower) to as high as 95 per cent. Adulteration of this commercial nicotine with ammonia and pyridine has been practiced, so that this must be remembered in determining the nicotine content of an insecticide, especially when such is in question in a forensic case.

There has been much discussion over the question of the presence of nicotine in tobacco smoke. It is undoubtedly true that tobacco smoke varies in character, according to the proportion of air admitted during combustion, the oxidation being more perfect in the case of cigarettes, somewhat less with cigars, and least in the case of pipe smoking.[2] In the smoke there have been found varying amounts of carbon dioxide, carbon monoxide, hydrogen sulphide, hydrocyanic acid, and pyridine, none of which have great meaning, in the amounts present, from the toxicological point of view, although the hemoglobin might become saturated with CO to the extent of 10 to 20 per cent. within an hour of continuous smoking. Melsens, with the confirmation of Kissling, seems to prove that as much as 1/7 of the original nicotine of the tobacco may be found in the smoke, while Lehmann, as well as Garner, show that somewhat more than 1/3 of the nicotine may be recovered from the smoke. Storm van Leuwen has investigated the actual nicotine content of cigar smoke collected under conditions comparable to those that prevail in the actual performance of smoking, and shows that the common distinction between so-called "mild" and "strong" cigars is no index of the nicotine that may pass into the smoke, nor could the color or even the nicotine content of the leaf be depended on to foretell the outcome of the actual smoke test. That the products of combustion are absorbed and produce untoward effects is well known from the experience of every smoker, the first cigar almost invariably producing marked toxic effects and continuing to produce them until tolerance is established. The relatively greater effects of inhalation of the smoke, as is common in cigarette smoking, are due to the greater and more active absorption of the decomposition products from the lungs. Baumberger shows that the average nicotine content of the smoke in per cent. weight of tobacco is 0.573 per cent. in the case of cigarettes. As cigarettes weigh about 1 gram each, and about 80 per cent. of the tobacco is smoked, the nicotine in the puffed smoke amounts to about 5 mg. for each cigarette. Of the nicotine in the tobacco from 14 to 33 per cent. appears in the smoke puffed. If the smoking of cigarettes is done continuously for 1 hour, the maximum amount of nicotine retained in the body is calculated by Baumberger as 36 mg. per hour in inhaling and 27.5 mg. per hour in puffing; while Heinz reports that, with inhalation of the smoke, 8 times more nicotine is absorbed than in smoking without inhaling.[1] Tedeschi calls attention to the tendency of excessive smoking to produce seizures resembling epilepsy, while Bates shows that smoking produces a slight temporary rise in blood pressure and heart rate.[2] Moschowitz[3] has shown that tobacco smoking may cause symptoms closely resembling the angina pectoris of coronary or aortic disease, and that there are two types of so-called "tobacco heart": (*a*) those in which there is no evidence of cardiac injury; and (*b*) those in which the signs are suggestive of the intraventricular conduction disturbance associated with coronary or aortic disease.

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[1] See "Denicotinized Tobacco" by Bailey, Nolan, and Mathis, Bull. 295, Conn. Agric. Exp. Station, 1928. Abstract in Jour. Amer. Med. Assoc., 1928, **91**, 583. See, also, Winterstein and Aronson, Schweiz. med. Wchnschr., 1929, **59**, 550; and Jour. Amer. Med. Assoc., 1929, **93**, 938.

[2] See Lee, Quart. Jour. Physiol., 1908, **1**, 335.

As far as we have found the literature contains record of 22 cases of nicotine poisoning as such, most of which were fatal.[4] There are many recorded cases of death from tobacco, which has been used as an infusion or decoction for external application, or as an enema. The use of tobacco as a snuff, or in the form of chewing tobacco has, likewise, resulted in death, as has, also, the accidental introduction of tobacco into the food. Several cases have been cited of the use of tobacco or of nicotine with homicidal intent, one of these being the poisoning of Fougnies by Count Bocarmé, in investigating which Stas first used his process for separating alkaloids from organic mixtures.[5]

Properties.—Nicotine is a rather strong di-acid, ditertiary base, forming salts with one or two equivalents of acid. It has the formula $C_{10}H_{14}N_2$, and is a derivative of both pyridine and pyrrolidine with the chemical name β-pyridyl-α-n-methylpyrrolidine, its structural formula being represented as follows:

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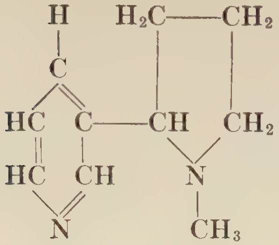
[1] See Kissling, Ding. Polyt. Jour., 1882, **244**, 64; Lehmann, Münch. med. Wchnschr., 1908, **55**, 723; Garner, Bull. 141, U. S. Dep't. Agric., Bureau of Plant Ind., 1909; Bush, New York Med. Jour., 1914, **99**, 519; Storm van Leuwen, Arch. f. exp. Path. u. Pharm., 1918, **84**, 282; Editorial, Jour. Amer. Med. Assoc., 1919, **73**, 108; Asherson, Chem. News, 1919, **120**, 150; Hirschfelder, Lange and Feaman, Science, 1920, **51**, 21; Hahn and Langer, Ztschr. f. Hyg. u. Infektionskr., 1920, 90, 22; Baumberger, Jour. Pharm. & Exp. Therap., 1923, **21**, 35 and 47; Heinz, Deutsche med. Wchnschr., 1923, **49**, 318; Binet, Presse méd., 1925, **33**, 134.

[2] Tedeschi, Riforma Med., 1917, **33**, 169; Bates, Jour. Comp. Psych., 1922, **2**, 431. For a discussion of the subject of tolerance to nicotine see Edmunds, Jour. Pharm. and Exp. Therap., 1909, **1**, 1; Dixon, Proc. Royal Soc. of Med., 1911, **5**, 1; Dixon and Lee, Quart. Jour. Exp. Physiol., 1912, **5**, 373; Edmunds and Smith, Jour. Lab. & Clin. Med., 1916, **1**, 315; Armstrong and Evans, Brit. Med. Jour., 1922, **1**, 992.

[3] Jour. Amer. Med. Assoc., 1928, **90**, 733.

[4] For bibliography see "Alkaloidal Poisons" by Prescott and Webster in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 559.

[5] Stas, Bull. acad. roy. de méd. de Belg., 1851–52, **11**, 202.



Pure nicotine is a colorless, oily fluid with little odor, but with a sharp, burning taste. On standing, or on dissolving in water, it assumes the peculiar smell of tobacco. On exposure it gradually darkens in color, becoming deep brown, and is eventually changed to a resinous mass. It boils, without decomposition, at 246.7°C. under a pressure of 745 mm. Its specific gravity at 20°C. is 1.0092. It is strongly levorotatory, its specific rotatory power at 20°C. being -168.40 to -168.66, according to Jephcott.[1] Its refractive index at 20°C. is 1.53, that of the commercial 95 per cent. nicotine used as an insecticide being 1.525, according to Fryer and Fryer.[2] It is capable of distillation, without decomposition, with steam or in a vacuum. It is soluble in water, alcohol, amyl alcohol, ether, petroleum ether, benzene, chloroform, and oils. Its aqueous solution is strongly alkaline in reaction, and differs from similar solutions of coniine as discussed on page 614. In the absence of other basic substances, it may be easily determined by titration with standard acid, using methyl red, methyl orange, cochineal, or iodeosin, as indicators, 1 cc. of N/50 sulphuric acid being equal to 0.003246 gram of nicotine. The monacid salts of nicotine are stable and neutral to litmus and methyl orange, but the diacid salts have an acid reaction. Most of the salts of nicotine crystallize with difficulty, the acid tartrate being an exception.

Symptoms.—Poisonous doses of nicotine produce a hot, burning sensation in the mouth, which spreads down the esophagus to the stomach. This is followed by sweating and salivation, nausea, vomiting, pain in the abdomen, and, occasionally, purging. There is, ordinarily, considerable vertigo, headache, disturbances of sight and speech, some mental confusion, great muscular weakness, and restlessness. Clonic convulsions appear later, accompanied by fibrillary twitching of various muscles, and, later, tetanic spasms may appear, the convulsions, in some cases, being followed by complete relaxation of all parts of the body with loss of the reflexes. The respiration is quick, deep, and labored; the blood pressure is at first increased and later diminished; while the pulse is generally slow at first, and then becomes very rapid, although after very large doses acceleration may be noted at first, and later slowing and weakening of the pulse. The pupils are, usually, narrowed, at first, but become dilated later. Death is due to respiratory paralysis, the heart continuing to beat after respiration ceases. If the dose be very large, death may be sudden from paralysis of the central nervous system.

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[1] Jour. Chem. Soc., 1919, **115**, 104.

[2] Analyst, 1919, **44**, 363.

Fatal Dose.—In the reported cases large doses of nicotine have been taken, so that it is a difficult matter to state just what is the minimum lethal dose. Kobert[1] states that the smallest fatal dose for an adult is not greater than 0.06 gram, which is confirmed by Erben.[2] It is highly probable that 3 or 4 drops of the pure alkaloid would cause death, although recovery may follow such or higher doses in those who have become very tolerant to the effects of tobacco. Death has followed the internal ingestion of 0.8 gram of snuff-tobacco, while an infusion of 2 grams of dry tobacco used as an enema has caused death. In the cases of McNally[3] two persons drank about 30 cc. each of an insecticide containing 39.84 per cent. nicotine.

Fatal Period.—The symptoms of nicotine poisoning begin as soon as a poisonous dose reaches the circulation. Very large doses may prove fatal within a few seconds. The course of the poisoning in fatal cases is a very rapid one, measured by minutes rather than by hours. It may cause death without any subjective symptoms, in one reported case of suicide the subject falling dead with the vial from which he had taken the poison still in his hand.[4] In the celebrated Bocarmé case,[5] death occurred in five minutes, as did the two cases reported by McNally[6]. In the reported cases of death from tobacco, the period of death is somewhat slower in appearing than with pure nicotine. Sonnenschein[7] reports the cases of 2 suicides who died in 3 and 5 minutes respectively after swallowing 1 or 2 ounces of tobacco. Grahl[8] describes a case of death following the administration of a decoction of 1 ounce of tobacco in ¾ hours.

Treatment.—The treatment of cases of poisoning with nicotine or tobacco consists in the evacuation and lavage of the stomach, and the administration of finely pulverized charcoal partially to absorb the alkaloid. Lorenz[9] recommends the addition of tannic acid or a solution of iodine in potassium iodide to the lavage water, and advises the trial of dilute hydrogen peroxide. The toxic effects are to be met by stimulants, friction rubs, and warmth, promotion of the respiration, and the inhalation of oxygen.

Postmortem Appearances.—There is little characteristic in the findings, except, possibly, when the odor of tobacco may be present in the stomach or pervading the whole body. The blood is dark and fluid.

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[1] *Lehrbuch der Intoxikationen*, 2te. Aufl., 1906, **2**, 1064.

[2] Cited by Starkenstein, Rost and Pohl, *Toxikologie*, 1929, p. 427.

[3] Jour. Lab. & Clin. Med., 1920, **5**, 213. See, also, McNally, Ibid., 1922, **8**, 83.

[4] Harben Case, Pharm. Jour. and Trans., 1859–60, n. s. **1**, 195.

[5] Procès du comte et de la comtesse de Bocarmé devant la cour d'assises de Hainault. Mons., 1851. See, also, Stas, Bull. acad roy. de méd. de Belg., 1851–52, **11**, 202.

[6] *Loc. cit.*

[7] Cited by Weidanz, *Heilkunde*, 1907, p. 333.

[8] Jour. de Prak. Heilkde., 1830, **71**, 4 St., 100.

[9] Klin. therap. Wchnschr., 1909, **16**, 1298.

Congestion of the brain and internal viscera is usually found. If death has not occurred rapidly, signs of a more or less intense gastro-enteritis are observed.

Detection.—This may be done by the method outlined under coniine on page 614. This method is subject to both positive and negative errors; the first owing to the possible presence of ammonia or pyridine, or both, in the residues obtained; the second on account of the possibility of loss of substance, or incomplete extraction. If ammonia be present, it may be gotten rid of by treatment with oxalic acid as outlined under coniine. If pyridine be present, it may be separated from nicotine by submitting the residue to distillation in acetic acid solution, under which conditions the pyridine passes over in the distillate, the nicotine remaining behind. In the examination of insecticides especially, and, possibly, to a less extent in analyzing tissues, Graham and Carr[1] believe that the difficulty in obtaining a quantitative recovery of the nicotine is due to the probable formation of insoluble hypothetical combinations of calcium with nicotine, a view which is combated by Thatcher,[2] who believes the error is due to loss of nicotine in the preliminary steps of the analytical process. Dangelmayer[3] calls attention to the fact that trichlorethylene extracts nicotine quantitatively from alkaline solutions, and that the nicotine may be recovered by shaking this extract with dilute sulphuric acid. Having isolated the supposed alkaloid, it may be identified by the following tests.

1. *General Precipitants.*—Most of the general alkaloidal precipitants will precipitate nicotine from quite dilute solutions, a point of distinction from coniine. Silicotungstic acid or potassium silicotungstate, when added to a solution of nicotine containing an excess of free hydrochloric acid, yields an immediate precipitate at dilutions of 1:300,000, while at a dilution of 1 part of nicotine per million a crystalline precipitate appears on allowing the mixture to stand for 24 to 48 hours. Coniine, with this reagent, yields precipitates only at dilutions of 1:5000 or stronger.[4]

2. *Crystallization Test.*—If a few drops of nicotine be placed on a watch-glass and a few drops of concentrated hydrochloric acid on another watch-glass, one of these glasses being inverted over the other, a white cloud is produced, which is not so dense as in the case of coniine. With nicotine no crystals will be observed on the glasses, while with coniine a prompt appearance of characteristic crystals of coniine hydrochloride will be noted. If this test be made by evaporating a few drops of concentrated hydrochloric acid with a few drops of nicotine, a varnish-like residue will appear, which is amorphous, but which will change to a crystalline deposit on allowing it to stand over sulphuric acid for some

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[1] Jour. Amer. Chem. Soc., 1924, **46**, 695.

[2] Ibid., 1539.

[3] Chem. Ztg., 1918, **42**, 290; Abstract in Chem. Abs., 1919, **13**, 2958.

[4] See Sanchez, Semana Médica, 1921, **28**, 217.

time. With coniine, the formation of crystals is almost immediate. This test is more valuable in differentiating nicotine from coniine than it is in identifying nicotine.

3. *Roussin's Test.*—If an ethereal solution of iodine be added to an ethereal solution of nicotine, a brownish-red amorphous precipitate is produced, which, after standing for some hours, is converted into a crystalline mass of long, ruby-red needles, known as "Roussin's crystals". This reaction occurs at a dilution of about 1:100, while with more dilute solutions the amorphous phase of the reaction may be absent. If the nicotine be resinous, these crystals are formed with difficulty. No crystals are formed with coniine.

4. *Schindelmeiser's Test.*—If nicotine that is not resinous is treated with a drop of 30 per cent. formaldehyde solution, which is free from formic acid, and then with a drop of concentrated sulphuric or nitric acid, the mixture assumes an intense rose-red color. If the nicotine and formaldehyde be allowed to stand for several hours, a solid compound is formed, which gives a more pronounced color on the addition of nitric acid. If this latter technic be employed, the formaldehyde must not be in excess, otherwise the solution becomes green after a time and rapidly decomposes. This test is not given by coniine, trimethylamine, piperidine, pyridine, or aniline, nor by the ptomaines resembling nicotine.

5. *Tunmann's Test.*—Dissolve a few crystals of para-dimethylaminobenzaldehyde on a watch-glass in a drop of fuming hydrochloric acid, adding thereto from the side a drop of the aqueous solution of nicotine. A rose-red color develops immediately at the surface of contact, then a violet-red zone results, and, finally, the entire liquid becomes violet-red, the color increasing in intensity and persisting for 10 to 24 hours. Coniine and pyridine give no color with this reaction, while aniline yields in not too dilute solutions a red color, but immediately precipitates a dyestuff in the form of red needles.

6. *Biologic Test.*—If a very small amount of nicotine (1 cc. of a 1:1000 solution) be injected into the dorsal lymph-sac of the frog, the animal rapidly becomes uneasy, and in 5 to 10 minutes, or even less, assumes the following position: the forelegs are pressed backward against the sides of the body, and the hind legs are drawn up in such a position that the thighs are at right angles to the body, and the legs are fixed so that the feet rest upon the back. The respiration is at first accelerated and then becomes slow. Slight muscular spasms, especially in the hind legs, may be noted. With larger doses a severe clonic spasm results, followed by fixation of the legs in the position mentioned above, slowing or stoppage of respiration, fibrillary contractions, and general muscular relaxation.

Determination.—The best method of making a quantitative determination of the nicotine in the tissues is that of Bertrand and Javillier.[1] A weighed amount of the finely hashed organ, or a measured volume of the stomach contents or other fluid, is placed in a distilling flask and a sufficient amount of water and sodium hydroxide solution added to make the mixture of the consistency of thin gruel and strongly alkaline in reaction. A few pieces of glass or pumice may be placed in the flask to prevent bumping. Distillation is then carried out with a rapid current of steam in the usual manner, the distillate being collected in a large flask containing 15 or 20 cc. of 10 per cent. hydrochloric acid. Continue the distillation until a portion of the distillate shows no opalescence when treated with a few drops of 10 per cent. solution of silicotungstic acid followed by a few drops of hydrochloric acid. After the distillation is complete, make the distillate up to a definite volume and filter through a dry filter, testing a portion of the filtrate with methyl orange or methyl red to be certain that the reaction is still acid. Measure with a buret an aliquot part of the filtrate, allowing it to flow into a beaker or small flask. Add a few cc. of 10 per cent. hydrochloric acid (3 or 4 cc. for each 100 cc. of liquid taken), and follow this with a few cc. of 10 per cent. solution of silicotungstic acid[1], mix thoroughly and allow to stand for 18 to 24 hours. At the end of this time filter the crystalline precipitate through a quantitative known-ash filter, and wash with water containing a little hydrochloric acid. The original filtrate should be tested with a few drops of the nicotine distillate in order to insure an excess of the reagent in the original mixture, and, likewise, the washing should be continued until all of the excess silicotungstic acid is removed from the precipitate. After the washing is complete, transfer the filter and precipitate to a weighed platinum crucible, dry carefully, and incinerate first over an ordinary Bunsen lamp, and then over the blast lamp for a few minutes. Cool in a desiccator to constant weight. If the weight of the incinerated residue be multipled by 0.114 the product yields the amount of nicotine in the aliquot part of the filtered distillate taken for the determination. Proper calculation gives the total nicotine in the complete distillate, and likewise in the total original organ from which the portion was taken for the determination.

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[1] Bull. d. Sc. Pharmacol., 1909, **16**, 7; Bull. acad. roy. de med. de Belg., 1909, p. 1042; Bull. Soc. chim., 1909, **5**, 241.

NON-VOLATILE ALKALOIDS

This group comprises practically all of the important alkaloids, especially those used as remedial agents. These alkaloids are composed of carbon, hydrogen, nitrogen, and oxygen, and are, with few exceptions, colorless or white crystalline solids, odorless, and incapable of distillation without decomposition.

Aconitine

Most of the different species of Aconitum contain one or more characteristic alkaloids, although there is some similarity in the various alkaloids of the aconitine group. Chemical and physiologic properties divide the alkaloids of the Aconitum group into two classes: (1) the highly toxic aconitine ($C_{34}H_{47}NO_{11}$, derived from *Aconitum napellus*), pseudoaconitine ($C_{36}H_{49}NO_{12}$, from *Aconitum ferox*), japaconitine ($C_{34}H_{49}NO_{11}$, from *Aconitum Fischeri*, Hondo variety, sometimes called *Aconitum japonicum*), jesaconitine ($C_{40}H_{51}NO_{12}$, from *Aconitum Fischeri*, Kokkaido variety), lycaconitine ($C_{27}H_{34}N_2O_6.2H_2O$, from *Aconitum lycoctonum*), indaconitine ($C_{34}H_{47}NO_{10}$, from *Aconitum chasmanthum*), bikhaconitine ($C_{36}H_{51}NO_{11}$, from *Aconitum spicatum*), lapaconitine ($C_{34}H_{48}N_2O_8$, from *Aconitum septentrionale*); and (2) the practically inert alkaloids atisine ($C_{23}H_{31}NO_2$, from *Aconitum heterophyllum*), and palmatisine (formula unknown, from *Aconitum palmatum*). Although commercial aconitine may consist of a mixture of some of these alkaloids, depending on the drug from which the extraction is made, we shall limit our discussion to the official aconitine.[1]

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[1] McNally (Jour. Lab. & Clin. Med., 1920, **5**, 213) recommends 1 cc. for every 0.01 gram of nicotine suspected.

The official aconitine represents the poisonous alkaloids of *Aconitum napellus*, the three or four other bases in aconite being either non-toxic or much less toxic than aconitine. Although aconitine exists in all parts of the plant, the root contains it in greatest amount, and is the part from which the U. S. Pharmacopoeia directs that the official tincture shall be prepared (the extract and fluidextract of aconite, which were official in the preceding Pharmacopoeia, having been deleted from the present 10th revision). The total alkaloidal content of the good root is said to average from 0.175 to 1 per cent, but the percentage of absolute aconitine in the root cannot well be declared from the results of analysis, although, from data based on physiologic effects, it would appear that the poisonous power of aconite root is equivalent to not more than 0.01 to 0.02 per cent. of absolute aconitine. The standard of the present (10th revision) Pharmacopoeia is not based on the chemical factors, but rather upon a biologic property, the official statement running "Tincture of Aconite, administered subcutaneously to guinea pigs, has a minimum lethal dose of not less than 0.00,035 cc. and not more than 0.00,045 cc. for each Gm. of body weight of guinea pig."

The majority of cases of aconitine poisoning noted in the literature are accidental, 159 out of 195 by aconite and its preparations, and 19 out of 27 by aconitine itself; 27 cases of suicide from aconite are noted, and 16 authentic cases of homicide from aconite or aconitine are found in the literature.[2] According to Witthaus "In 60 instances the tincture or fluid extract was taken by the victim either without medical advice or through mistake in the directions; in 22 cases the liniment, intended for external use, was swallowed; in 15 instances the poisonings were caused by errors of pharmacists in compounding medicines. In 19 poisonings the root itself or a decoction of it was taken in mistake for some other root, usually for horseradish."

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[1] For the properties of the remaining aconitum alkaloids see Schmidt in Abderhalden's *Biochemisches Handlexikon*, 1911, **5**, 401 *et seq.*

[2] For bibliography see Witthaus, *Toxicology*, 1911, p. 850; and *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 439.

Properties.—Aconitine ($C_{34}H_{47}NO_{11}$) occurs as colorless or white crystals, those crystallized from alcohol appearing as rhombic prisms or plates. It is odorless, and is stable in the air. It is probable that the bitter taste of aconite is due to its amorphous alkaloids, rather than to aconitine. It reacts weakly alkaline to litmus; is readily soluble in chloroform and benzene (1 part in 7), less easily in alcohol (1 in 28), and in ether (1 in 65), very slightly in water (1 in 4431), and almost insoluble in petroleum ether. It is dextrorotatory, while its salts are levorotatory. If heated rapidly, it melts at about 195°C., giving off acid vapors, various specimens of the alkaloid differing in the melting-point. Aconitine is a very unstable alkaloid, readily undergoing hydrolysis or saponification, even by boiling with water. This hydrolysis takes place in two stages, the first stage being the conversion of aconitine into acetic acid and picraconitine, the latter then decomposing, in the second stage, into benzoic acid and aconine, an inert amorphous base with the formula $C_{25}H_{41}NO_9$. The exact graphic formula of aconitine is unknown, but it is known chemically as acetyl-benzoyl aconine. Dilute solutions of aconitine yield precipitates with mercuric-potassium iodide solution, phosphomolybdic acid, tannic acid, and gold chloride, but only concentrated solutions give precipitates with platinic chloride, mercuric chloride and trinitrophenol.[1] The precipitate with gold chloride is especially characteristic, being a yellow amorphous precipitate which may be crystallized from alcohol, either with 3 molecules of water or without water, in the form of needles or rectangular prisms of the formula $C_{34}H_{47}NO_{11}HCl.AuCl_3$, the form with water of crystallization melting at 136°C. and containing 19 per cent. of gold, while the anhydrous salt melts at 145°C. and contains 20 per cent. of gold.

Symptoms.—In poisonous doses the symptoms noted are tingling and numbness in the mouth, burning in the throat and stomach, salivation, nausea, usually followed by marked retching and vomiting, rarely purging, grinding of the teeth, numbness and tingling of the fingers and other parts of the body, pain in the eyes and head, mydriasis, difficulty in swallowing and sometimes in speaking. Cramps in the extremities, tetanic manifestations, and occasionally marked convulsions may be noted. The pulse from the first is slow, feeble, and irregular; the surface of the body is cold and moist; the face bloodless; and the strength prostrated. Delirium is unusual, and stupor rarely appears. The respiration is shallow, dyspneic, and rapid, but becomes slow as the case progresses. Death occurs from syncope or respiratory failure. In cases running a rapid course, the symptoms may resemble general shock.

Fatal Dose.—Pure aconitine is one of the most powerful poisons known. According to Gadamer[2] death has occurred from a dose of not quite 1 mg., while Busscher[3] reports the death of Dr. Meyer from a dose of approximately 4 mg., and Ipsen[1] gives 3 mg. as the lethal dose. In the case examined by McNally it was definitely established that 6 mg. (1/10 grain) was the fatal dose.[2]

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[1] See *U. S. Pharmacopoeia*, 10th Rev., 1925, p. 30.

[2] *Lehrbuch der chemischen Toxikologie*, 2te. Aufl., 1924, p. 514.

[3] Berl. klin. Wchnschr., 1880, **17**, 337 and 356.

Fatal Period.—The symptoms appear quickly, almost as soon as the poison reaches the circulation, and the course is rapid.[3] Death generally takes place in 3 or 4 hours, although it may not occur for a day or more. In the famous Lamson Case[4] death occurred about 3¾ hours after the capsule was given. In one series of 6 fatal cases reported by Mallet,[5] the shortest fatal period was 8 minutes and the longest was 4 days. The most rapidly fatal case appears to be that of Bennet[6] in which death occurred in less than 7 minutes after swallowing an unmentioned amount of the liniment.

Treatment.—This consists of evacuation of the stomach, accompanied by gastric lavage with water containing tannic acid and finely powdered charcoal to diminish the solubility of the alkaloid. Cardiac stimulants, such as digitalis and strychnine should be given, while threatened respiratory failure should be treated by artificial respiration, if necessary. The patient should be kept warm by the use of hot water bottles or hot baths.

Postmortem Appearances.—The findings at autopsy are not characteristic. The lungs, liver, kidneys, and brain are generally found somewhat congested. Effusions may be noted in the pericardium and in the ventricles of the brain. The stomach and intestines are, in some cases, hyperemic. The blood may be abnormally fluid, and sometimes of a bright red color.

Detection.—The elimination of aconitine takes place through the urine and saliva, so that these fluids are especially valuable for study. As the organs usually submitted for examination may contain this alkaloid, these should, also, be analyzed. In separating aconitine from the tissues, the process outlined on page 344 should be followed, special care being taken to prevent hydrolysis. The finely hashed tissue should be digested with dilute alcohol, preferably at room temperature for some time and then at a temperature not over 60°C. for an hour or so, the extracting fluid being made only *very slightly acid* with tartaric or acetic acid. After separating the fat by allowing the extracts to stand in the ice-box, the fat is removed and the filtrate is evaporated at a low temperature under a vacuum. Both ether and chloroform should be used as immiscible solvents, and alkalinization is to be carried out with sodium bicarbonate instead of the stronger alkalies.

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[1] Vrtljschr. f. ger. Med., 1914, 3f. **47**, 1 Supp., 180.

[2] Personal communication (March 1, 1917) from office of Coroner's Chemist, Chicago, Ill.

[3] See Lewin, *Gifte und Vergiftungen*, 1929, p. 601.

[4] Reg. *v.* Lamson, Central Criminal Court, Sessions Paper, 95, pt. 569, pp. 547–590; Stevenson, Guy's Hosp. Rep., 1883, 3s., **26**, 307; Review of Lamson Case, Brit. Med. Jour., 1913, **2**, 1306.

[5] Pharm. Jour. and Trans., 1883, 3 s., **13**, 901.

[6] Monthly Jour. Med. & Surg., 1852, **15**, 69.

While it has been stated that aconitine is non-resistant to putrefactive processes[1], Lewin[2] asserts that it is not altered under conditions of decay, and Palet[3] has shown that aconitine could be readily detected after a lapse of 2 months. The detection and identification of aconitine is not always the simplest matter, so that the conclusion of Haines[4] seems warranted, when he states: "If a small but fatal dose of the poison were to be given, especially if it were administered hypodermically, the chances of its detection in the body after death would not be great." The identification of aconitine rests, largely, upon physiologic tests, as the chemical reactions are not especially characteristic, although certain of them may give strong confirmatory evidence.

Biologic Tests.—In preparing the solution for these tests, dissolve a little of the residue, obtained from the final ether extraction, in water slightly acidulated with acetic acid, filter, neutralize the filtrate with sodium carbonate solution, and dilute to 5 cc. with water. Dip a piece of filter paper in this solution and apply the moistened paper for a short time to the tip of the tongue. If aconitine be present, a numbness and tingling of the tongue will be noticed in 5 to 10 minutes, or, if the solution be very concentrated, a burning sensation is noticeable. Care should be taken to avoid excess of aconitine in this test. The symptoms may persist for several hours, and a 1:100000 solution will produce the effects mentioned. Instead of using this test upon the human being, the action of the residue may be tested upon the isolated heart of the frog, or given hypodermically to a mouse or frog. If a portion of the solution prepared as above mentioned be injected hypodermically into a mouse, or into the lymph-sac of a frog, the animal will die, usually within an hour, a test that is not, of course, especially characteristic of aconitine. If a small portion of the alkaloidal residue be prepared as for the test upon the tongue, except that the final dilution is made with Ringer's solution instead of water, and applied to the isolated frog's heart, a cardiographic tracing will show 3 stages, (1) a preliminary quickening of the beat; (2) tetanization of the cardiac muscle followed by a peculiar wave-like action (peristalsis); and (3) final arrest in diastole. The second stage is especially characteristic of the action of aconitine.[5]

Chemical Tests.—The properties of aconitine have been given on page 625. The formation of the crystalline chlor-aurate, and the determination of its melting point and percentage of gold offer considerable confirmatory value to the biologic tests.[6] A small portion of the solid residue, obtained in the extraction processes, dissolves in concentrated sulphuric or nitric acid without color, or, at most, with a slight yellow coloration. If a portion of the solid residue be treated with a few drops of Mandelin's reagent (a 1 per cent. solution of ammonium vanadate in concentrated sulphuric acid), an orange color is produced in the presence of aconitine. Pure aconitine does not give Vitali's test (see atropine), but pseudoaconitine, which may be present along with aconitine, does give this reaction.

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[1] Vibert, *Précis de Toxicologie*, Paris, 1915, p. 695.

[2] *Lehrbuch der Toxikologie*, 1903, p. 570; *Gifte und Vergiftungen*, 1929, p. 604.

[3] Semana Med., 1919, **26**, 166 and 424.

[4] Hamilton's *System of Legal Medicine*, 1894, **1**, 423.

[5] See Fühner, *Nachweis und Bestimmung von Giften auf biologischem Wege*, 1911, p. 102; also Fühner, Arch. f. exper. Path. u. Pharm., 1911, **66**, 179.

[6] See Carel, St. Paul Med. Jour., 1906, **8**, 666; also, Magill, Med. News, 1902, 1019, relative to the Condon Case.

Alvarez's Reaction.[1]—Place a portion of the purified solid residue, obtained in the extraction processes, in a small porcelain dish and add 5 to 10 drops of pure bromine. Heat on the water-bath, add 1 to 2 cc. of strong nitric acid, and evaporate to dryness again, adding a few drops more of bromine if the nitric acid loses its color. To the yellow oxidation product thus formed add ½ to 1 cc. of a saturated alcoholic solution of sodium hydroxide, and again evaporate to dryness. A red or brown residue is obtained depending on the amount of aconitine present. Allow to cool and add 5 to 6 drops of a 10 per cent. aqueous solution of copper sulphate, when a beautiful deep green color is observed if aconitine be present. None of the ordinary alkaloids were found by Alvarez to give this reaction.

Palet's Reaction.[2]—Place a portion of the purified solid residue in a small porcelain dish, and add a few drops of a mixture consisting of 25 grams of concentrated ("syrupy", 85 per cent) phosphoric acid and 1 gram of sodium molybdate. Heat directly over a small flame until vapors appear, when a very brilliant violet color is formed in the presence of aconitine. According to Palet only aspidospermine and veratrine give similar colors, and these alkaloids may be distinguished by other reactions.

Atropine and Related Alkaloids

The atropine series of alkaloids embraces a number of closely related bases, of which the most important are atropine, hyoscyamine, scopolamine, and atroscine. They are found in various parts of several plants of the solanaceae family (often occurring together), among which are *Atropa belladonna* (deadly nightshade), *Datura stramonium* (thorn-apple, Jamestown or jimson weed), *Hyoscyamus niger* (henbane), *Duboisia myoporoides*, and *Mandragora officinale* (mandrake). While other alkaloids, such as duboisine, mandragorine, and daturine, have been described, these are, probably, simply mixtures of the chief alkaloids. Certain basic substances, however, such as atropamine (apoatropine), belladonnine, and bellatropine, are occasionally found in these solanaceae, but do not have any special toxicologic value.

Atropine and its sulphate, and the hydrobromides of hyoscyamine and of scopolamine are official. While these solanaceous alkaloids exist in all parts of the plant, the Pharmacopoeia directs that the official parts of these plants are the dried leaves and tops, as well as the dried root, of *Atropa Belladonna* (most of the official preparations being prepared from the leaves, although there is, also, a fluidextract of the root), the dried leaves, with or without the tops, of *Hyoscyamus niger*, and the dried leaves and flowering tops of *Datura stramonium.*

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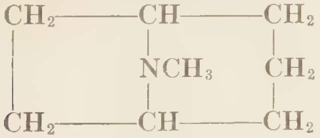
[1] Chem. News, 1905, **91**, 179.

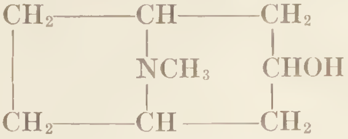
[2] Jour. pharm. chim., 1919, **19**, 295.

The large majority of cases of poisoning with the atropine series of alkaloids is accidental, suicidal and homicidal cases being relatively rare. Thus, of 383 cases of belladonna poisoning, 303 were accidental, 9 suicidal, 6 homicidal, and 65 of uncertain origin; of 317 cases of atropine poisoning, *per se*, 252 were accidental, 29 suicidal, 8 homicidal, and 28 uncertain; of 273 cases of stramonium poisoning, 186 were accidental, 3 suicidal, 12 homicidal, and 72 uncertain; of 55 cases of hyoscyamus poisoning, 27 were accidental, 1 suicidal, 4 homicidal, and 23 uncertain; of 35 cases of scopolamine poisoning, 33 were accidental and 2 suicidal. Recovery was the rule in these cases, of the 1063 above mentioned, 112 or approximately 10½ per cent. were fatal.[1]

Properties.—While the various members of the atropine family of alkaloids show much similarity, both in their toxicological and chemical properties, yet their recognition and differentiation is possible owing to certain chemical attributes possessed by each of them. It is probably true that the young plants contain, as a rule, hyoscyamine and scopolamine, and that these are readily changed to atropine and atroscine in the plant cells as the plant becomes older. Further, these alkaloids may be changed into one another in the processes of extraction, or even by allowing the preparations to stand, hyoscyamine, for instance being converted into atropine under the influence of hydroxyl ions in alcoholic solution. In aqueous solution hydrolysis or saponification takes place, more or less readily, into the acid and basic elements of which the alkaloids are composed. Through the influence of dehydrating agents, water is extracted from the acid portion of the molecule, such compounds as apoatropine. for instance, being formed.

As shown by saponification of the alkaloids of this group by heating with water, acids or strong alkalies, the atropine series are ester-like combinations of an aromatic acid with a base known as tropine ($C_8H_{15}NO$), while scopolamine is an ester of an aromatic acid with the base scopoline ($C_8H_{13}NO_2$), sometimes called oscine. Tropine belongs to the tropanering system of alkaloids, which consists of a peculiar combination of a 6 atomic group (pyrrolidine) with a 5 atomic group (piperidine) forming a complex derivative with a peripheral 7 carbon atomic ring:


Tropane


Tropine

Tropine is optically inactive and crystallizes from absolute ether in large plates, which melt at 63°C. It is very readily soluble in water and alcohol. Owing to the optical inactivity of the base tropine, the difference in rotatory power of atropine and hyoscyamine, which are isomeric, must be due to the acid element. The acid esters of the base tropine are known as tropeines.

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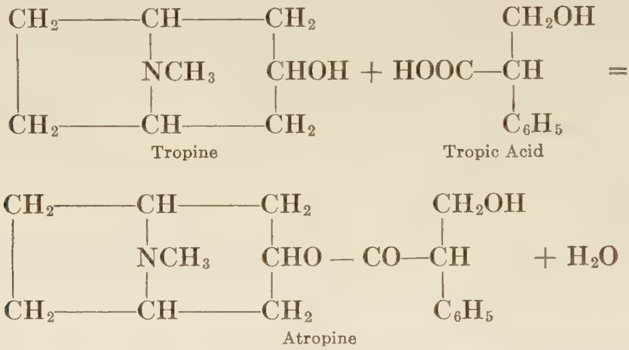
[1] For bibliography see Witthaus, *Toxicology*, 1911, p. 866 *et seq.*; also, *Legal Medicine and Toxicology* by Peterson, Haines & Webster, 1923, **2**, 451 *et seq.*

Atropine ($C_{17}H_{23}NO_3$).—This alkaloid is the chief one of *Atropa belladonna,* although hyoscyamine is present in varying amount together with much smaller quantities of scopolamine, atropamine, and belladonnine. Chemically, atropine is a tropeine, consisting of a combination of tropine with tropic acid ($C_9H_{10}O_3$), hence called tropine tropate, which is graphically represented as follows:



If tropic acid be heated with dehydrating agents it loses a molecule of water and becomes atropic acid, $C_9H_8O_2$. This latter acid forms with tropine the base apoatropine, which is occasionally found in belladonna. Inasmuch as hyoscyamine is readily converted into atropine by heating to 110°C. in absence of air, or by simply allowing an alcoholic solution to stand after addition of a few drops of alkali, it is a difficult matter to state just how much atropine and hyoscyamine are originally present in the crude drug.

Hyoscyamine and atropine are isomeric, but the former is optically active (levorotatory), while the latter is optically inactive. As both contain the base tropine, which is inactive, it follows that the optical activity of hyoscyamine is due to the acid element. Hyoscyamine, on hydrolysis with water, splits into tropine and tropic acid, the latter being levogyrate. If this saponification be made with acids or alkalies, the active tropic acid becomes inactive and assumes the racemic form, giving the same splitting products obtained from atropine. It follows, therefore, that atropine is simply a racemic modification, being correctly styled the racemic tropic acid ester of inactive tropine, while hyoscyamine is, chemically speaking, the levo-tropic acid ester of inactive tropine.

Atropine crystallizes from alcohol or chloroform in white, odorless, rhombic plates, which are optically inactive and melt between 114° and 116°C. One gram dissolves[1] in 455 cc. of water at 25°C. and in 90 cc.

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[1] The solubilities of the alkaloids and their salts are given as stated in the U. S. Pharmacopoeia, 10th Revision, 1925.

of water at 80°C.; in 2 cc. of alcohol at 25°C. and 1.2 cc. at 60°C.; in about 27 cc. of glycerin; in 1 cc. of chloroform; and in 25 cc. of ether at 25°C. Readily soluble in amyl alcohol and benzene, but very sparingly soluble in petroleum ether. Its saturated aqueous solutions are alkaline to litmus and to phenolphthalein. It is precipitated from its acidified solutions by the general alkaloidal reagents, van der Heyde[1] recommending Mayer's reagent as the most delicate and reliable for detecting atropine in small quantities of blood-serum. With gold chloride it produces, when in dilute HCl solution, a characteristic lusterless precipitate of atropine-gold-chloride ($C_{17}H_{23}NO_3HClAuCl_3$), the precipitate first appearing as an oil, but soon becoming crystalline. This salt melts at 135° to 137°C., and yields 31.35 per cent. of gold on combustion.

Atropine sulphate, $(C_{17}H_{23}NO_3)_2H_2SO_4$, the only official salt of this alkaloid, occurs as a white, odorless, crystalline powder, efflorescent in dry air. One gram of this salt is soluble in 0.4 cc. of water, 5 cc. of alcohol, 2.5 cc. of glycerin, 420 cc. of chloroform, and in 3000 cc. of ether, at 25°C.; also in 2.5 cc. of boiling alcohol. Its aqueous solutions are neutral to litmus. As usually found, it melts between 188 and 191°C., but when anhydrous and free from hyoscyamine it melts between 181 and 183°C., although, according to Richmond[2], it is stated to melt at 194°C.

Homatropine ($C_{16}H_{21}NO_3$).—This tropeine is an artificial or synthetic alkaloid obtained by the condensation of tropine with mandelic acid ($C_8H_8O_3$) in the presence of hydrochloric acid. It is known, therefore, as tropine mandelate and is the next lower homologue of atropine, hence the name homatropine. It crystallizes from absolute ether in prisms, which are very hygroscopic and melt between 95.5 and 98.5°C. The alkaloid itself is not used in medicine, the official salt being the hydrobromide. This latter compound ($C_{16}H_{21}NO_3HBr$) occurs as a white, odorless, crystalline powder, or in rhombic prisms. One gram is soluble in 6 cc. of water, 40 cc. of alcohol, and in 420 cc. of chloroform, at 25°C.; also in 12 cc. of alcohol at 60°C.; insoluble in ether. Its aqueous solution is neutral to litmus. The salt melts at about 212°C. with partial decomposition. The general alkaloidal reagents, with exception of tannic acid and platinic chloride, precipitate it from its dilute aqueous solutions. The alkaloid responds to Gerrard's and Arnold's tests, but not to Vitali's and Wasicky's tests. The chlor-aurate melts at 142 to 145°C.

Hyoscyamine ($C_{17}H_{23}NO_3$).—This alkaloid is the chief basic substance of *Hyoscyamus niger*, but is, also, present in varying amounts in belladonna and stramonium. It is isomeric with atropine, into which it is easily converted. Like atropine it is a tropeine, being a combination of tropine with levotropic acid, while atropine is a racemic modification of tropine with tropic acid, containing equal parts of the dextro- and levorotatory forms of hyoscyamine. Chemically speaking, therefore, hyoscyamine is the levotropic acid ester of inactive tropine.

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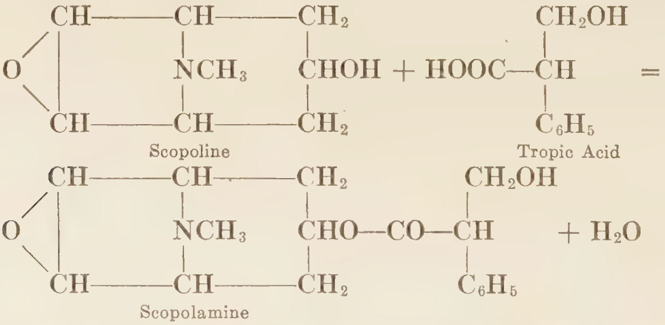
[1] Jour. Lab. and Clin. Med., 1922, 7, 280.

[2] Amer. Jour. Pharm., 1918, 90, 661.

Hyoscyamine is not official at the present time. It crystallizes from alcohol or benzene in needles, which have a melting point of 108.5°C. It is difficultly soluble in water, readily soluble in alcohol, ether, amyl alcohol, chloroform, and benzene. Its aqueous solutions are alkaline to litmus and phenolphthalein. It is levorotatory, showing a specific rotation at 15°C. of -20.3. Like atropine, it is precipitated from its acidulated solutions by the general alkaloidal precipitants, with exception of platinic chloride. With gold chloride it produces, when in dilute hydrochloric acid solutions, a characteristic precipitate of lustrous golden-yellow scales of hyoscyamine-gold-chloride ($C_{17}H_{23}NO_3HClAuCl_3$), melting at 162°C., and yielding 31.35 per cent. of gold.

The official hyoscyamine hydrobromide ($C_{17}H_{23}NO_3HBr$) occurs as white, odorless, deliquescent, prismatic crystals. This salt is very soluble in water. One gram is soluble in 2.5 cc. of alcohol, 1.7 cc. of chloroform, and in 2260 cc. of ether, at 25°C. Its aqueous solution is neutral to litmus and is strongly levorotatory. It melts at about 152°C.

Scopolamine ($C_{17}H_{21}NO_4$), also known as hyoscine, differs from other members of this series in not being a tropeine. Although a derivative of tropic acid, the base in combination is scopoline ($C_8H_{13}NO_2$) instead of tropine. This alkaloid is, therefore, scopoline tropate, and is represented by the following formula:



While scopolamine corresponds to hyoscyamine in being levorotatory, the racemic modification of scopoline with inactive tropic acid is known as atroscine, which corresponds with atropine.

Scopolamine is found in belladonna, stramonium, and hyoscyamus, as well as in the unofficial *Scopolia japonica.* It is an amorphous substance, difficultly soluble in water, but soluble in alcohol, ether, chloroform, and benzene. It is precipitated from its aqueous solutions by most of the general alkaloidal reagents. With gold chloride it produces, when in dilute HCl solution, scopolamine-gold-chloride ($C_{17}H_{21}NO_4$-$HClAuCl_3$), which crystallizes in large rhombic prisms, melting at 198 to 199°C., and yielding 30.65 per cent. of gold.

The official hydrobromide ($C_{17}H_{21}NO_4HBr.3H_2O$) occurs in colorless, transparent, rhombic crystals, sometimes of large size, which are odorless, and slightly efflorescent. One gram is soluble in 1.5 cc. of water and in 20 cc. of alcohol, at 25°C. It is slightly soluble in chloroform, but insoluble in ether. Its aqueous solution is neutral or at most only slightly acid to litmus. When anhydrous it melts at 190 to 192°C. It is levorotatory, its specific rotation at 25°C. in an aqueous solution containing the equivalent of 5 grams of the anhydrous salt in 100 cc. of solution and using a 100 mm. tube is not less than $-22°$ and not more than $-25.75°$.

Symptoms.—The symptoms of poisoning by belladonna, hyoscyamus, and stramonium are much the same, although the predominance of certain of the symptoms may vary with the different drugs, depending on their actual content of the characteristic alkaloids. The leading symptoms are: marked dryness of the mouth and throat, due to paralysis of the terminations of the chorda tympani nerve, which leads to marked diminution of the saliva; redness of the tongue; huskiness of the voice; thirst; difficulty in swallowing. There is wide dilatation of the pupils, due to paralysis of the myoneural junctions in the circular muscle of the iris, although a few cases are reported in which there was no dilatation[1]; the eyes are prominent, brilliant, wild and staring; there is impaired vision and loss of all accommodation, while the intraocular pressure appears to be unchanged in the normal eye, although the pressure may be increased, when there is already a tendency to increased pressure. The central nervous system is first strongly stimulated and later depressed, the action being largely exerted upon the motor areas. This action may result in hallucinations, giddiness, and vertigo, marked excitement, which may be silent and muttering, but is usually violent, the patient becoming belligerent, although he may, occasionally, be simply hilarious. This excitable stage may be associated with chorea-like movements or convulsions. The stimulant action passes from above downward, so that the medullary centers, as well as the cord, may be involved. Following the stimulant stage, the depression follows and may be so marked that almost complete paralysis of the central nervous system obtains. Respiration becomes quicker and deeper, frequently interrupted by convulsive movements of the respiratory muscles, and later becomes dyspneic, slower, and may finally cease. Nausea is common, and vomiting is not unusual. Upon the bowels atropine usually exerts a sedative action, the peristaltic movements being diminished, although Allan[2] reports a case in which belladonna caused marked diarrhea with cramping. These solanaceous alkaloids seldom cause little change in the output of urine, except in so far as they diminish the other secretions, the urine, however, being usually retained, although, at times, it may be freely voided[3]. The pulse is at first full and bounding, but becomes feeble and rapid, and sometimes intermittent and even imperceptible, owing to the paralysis of the terminations of the vagus in the cardiac musculature. The skin is dry and hot, due to paralysis of the nerve terminations in the sweat glands, but cases are reported in which the skin becomes cool soon after the toxic symptoms are established. A deep-red erythema may be observed on the skin. In some cases, especially in children, a febrile temperature may be observed as a "by-effect" of atropine[1]. A leukocytosis may be observed[2]. The picture ends with the paralytic stage, coma, asphyxia, convulsions, and death. Although the symptoms of atropine poisoning resemble, to some extent, those of other drugs, or of conditions such as botulism, yet, as a rule, the complex is so characteristic that this type of poisoning may, ordinarily, be recognized with a fair degree of certainty.

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[1] See Ghose, Indian Lancet, 1905, **25**, 125; McNally, Jour. Amer. Med. Assoc., 1915, **65**, 1640.

[2] Jour. Amer. Med. Assoc., 1928, **90**, 540.

[3] See Stalberg, Amer. Jour. Med. Sci., 1904, **127**, 517.

The **toxic effects of hyoscyamine** are practically the same as those of atropine given above, differing in degree rather than in the complex, as the former is rarely pure being changed into atropine, to some extent, when in solution. The narcotic influences attributed to hyoscyamine are due to the presence of scopolamine as an impurity and not to the hyoscyamine itself. Hyoscyamine acts almost twice as strongly as atropine on the peripheral nervous end-organs, while its influence on the central nervous system is the same. This is explained by Cushny[3] as follows: "The action of atropine, as has been stated, is compounded of that of natural or levorotatory hyoscyamine with that of its dextrorotatory isomer. The latter does not exist free in nature and possesses little or no action on the nerve terminations, while it stimulates the spinal cord of the frog more than either atropine or hyoscyamine. The peripheral action of atropine is thus due to its containing hyoscyamine, and as a grain of atropine contains only half a grain of hyoscyamine, the former naturally exercises only half the effect of a grain of hyoscyamine. On the other hand, the half grain of dextrorotatory hyoscyamine in a grain of atropine is almost inert on the nerve terminations, but exercises the same effect on the central nervous system as its levorotatory complement. Atropine thus acts on the central nervous system in mammals in the same strength as hyoscyamine, but only half as strongly in the periphery." Although hyoscyamine shows a stronger action in some respects than does atropine, the larger dose of the similar pharmacopoeial preparations of hyoscyamus, as compared with those of belladonna, is attributable to the lesser alkaloidal content of the former.

The **effects of scopolamine (hyoscine)** are similar to those of atropine, except that it depresses the central nervous system more markedly than does the latter, while its peripheral action is about the same as that of hyoscyamine, but passes off more quickly. Scopolamine poisoning shows its greatest variation from that of the tropeines in the usual nervous symptoms observed. Thus, there is a marked sensation of fatigue and drowsiness; patient becomes quiet, moves and speaks less, and soon falls asleep, the sleep resembling natural sleep and lasting 5 to 8 hours. In some cases, however, the stage of excitement noted with atropine may precede the sleep, de Villaverde[1] reporting 4 cases after such small doses as 10 drops of a 1:1000 solution of the hydrobromide, although such symptoms are especially noted after large doses, when they may be indistinguishable from those due to atropine. Scopolamine does not seem to be as dangerous as the other members of this group, while a certain degree of tolerance may be acquired by its use. This drug is used in combination with morphine in producing the so-called "twilight sleep", an association which has caused many toxic effects, although few deaths have been reported.

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[1] See White, Amer. Jour. Dis. Child., 1929, **37,** 745; Munns, Jour. Amer. Med. Assoc., 1929, **93,** 171.

[2] See Benzing, Monatschr. f. Kinderhkde., 1923, **24,** 509; Backman, Edstrom, Grabs, and Hultgen, C. R. Soc. de biol., 1925, **93,** 190.

[3] *Pharmacology and Therapeutics,* 9th Ed., revised by Edmunds and Gunn, 1928, p. 349.

Fatal Dose.—Recovery occurs in the majority of cases of poisoning from these solanaceous alkaloids, according to Falck, quoted by Kobert[2], 88.4 per cent. of the cases collected recovering. Kobert[3] gives as the minimal lethal dose for the adult 130 mg. of atropine, Starkenstein, Rost and Pohl[4] state this figure as 0.1 gram, Gadamer[5] says that 0.01 to 0.06 gram of atropine may cause death, and Hofmann-Haberda[6] ascribes a fatal action to 7 to 8 cg. of atropine. Much smaller doses of atropine have, however, caused death. The smallest quantity of atropine known to have caused death, in so far as we find in the literature, is 0.0004 gram instilled into the eye of a four year old child.[7] Arnold[8] reports a death from the hypodermic administration of 0.002 gram (1/30 grain) of atropine; Fabris[9] cites a case of death of an adult from 0.003 gram; Dunlap[10] relates the death of a patient in 41 hours from a dose of 0.004 gram (1/16 grain); and Jaenicke[11] records the death of a woman from 0.005 to 0.007 gram of the sulphate taken in divided doses during the night. While such small quantities have proven fatal, much larger doses have been recovered from, Macchiavelli[12], for instance, reporting recovery following intake of 0.5 gram of atropine sulphate. External application of atropine or of preparations of belladonna or hyoscyamus, may produce toxic results. Although the usual fatal dose of the berries of *Atropa*

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[1] Siglo Med., 1928, **81**, 137.

[2] *Lehrbuch der Intoxikationen,* 2te. Aufl. 1906, **2**, 1043.

[3] *Loc. cit.*

[4] *Toxikologie,* 1929, p. 421.

[5] *Lehrbuch der chemischen Toxikologie,* 2te. Aufl., 1924, p. 605.

[6] *Lehrbuch der gerichtlichen Medizin,* 11te. Aufl., 1927, p. 915.

[7] Burrenich, Ann. et bull. Soc. méd. de Gand., 1891, p. 288.

[8] Baltimore Med. Jour., 1871, p. 169.

[9] Quoted by Modica, Gazz. d. osp., 1898, **19**, 683.

[10] Amer. Pract. and News, 1887, n. s. **3**, 230.

[11] Deutsch. Arch. f. klin. Med., 1877, **20**, 617.

[12] Gazz. med. ital. lomb., 1880, **2**, 339; see, also, Meyer, Corr.-Bl. f. Schweiz. Aerzte, 1905, **35**, 548; Heller, Jour. Amer. Med. Assoc., 1929, **92**, 800.

belladonna is stated as from 3 to 10 berries, yet recovery has occurred after intake of 20, and even 50, of these berries.[1]

Concerning the lethal dose of the other solanaceous alkaloids little is known. Relatively large doses have been recovered from, while much smaller doses have proven fatal. Kobert[2] states that 12 fatal cases of scopolamine poisoning have resulted in 1200 cases of scopolamine-morphine anesthesia, one case reported by Ely[3] following after the administration of ⅛ grain of morphine with 1⁄100 grain of scopolamine hydrobromide. No fatal cases have occurred from the use of homatropine, although 20 non-fatal cases are recorded in the literature.

Fatal Period.—The symptoms of poisoning usually appear within an hour after the drugs have been taken into the stomach. The course of the poisoning is, as a rule, not especially rapid, in a majority of the fatal cases death occurring within 24 hours after ingestion of the poison, although it may be delayed for days.

Treatment.—The stomach should be washed out with copious amounts of fluid containing tannic acid or strong tea. Instead of tannic acid, a few drops of the compound solution of iodine may be employed to precipitate the alkaloids, or finely divided charcoal may be used to absorb the alkaloids and retard their absorption into the system. The general symptoms should be treated by subcutaneous administration of pilocarpine hydrochloride (10 mg., ⅙ grain), repeated, if necessary, until the mouth is moist. For the excitement and delirium, bromides may be employed, and ice caps applied to the head. Morphine, being a physiologic antagonist to atropine, may be administered *with caution*, but it must be remembered that morphine is a respiratory depressant and may be dangerous when the depressant effects of atropine are manifest. In the depressant stage, collapse should be combated by the use of caffeine or strong coffee, and artificial respiration vigorously employed.

Postmortem Appearances.—The findings at autopsy are not at all characteristic, as they are, practically, those following death from asphyxia. Externally the skin may show evidence of the peculiar rash associated with atropine poisoning, although this is rarely reported. The pupils are usually found dilated, even for many hours after death,[4] although, in some cases, no dilatation may be noted.[5] The lungs are usually congested or edematous, although there may be simply a hypostatic congestion. The pleural cavities may contain considerable serum. The blood may be found largely in the venous side of the circulation, the right heart be engorged, while the left heart may be relatively empty. The meninges and brain tissue are markedly congested. The throat, trachea, and esophagus may be hyperemic, while the mucous membrane of the stomach and small intestine may be congested, especially if the seeds or other parts of the plant have been ingested.

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[1] See Gadamer, *Lehrbuch der chemischen Toxikologie*, 2te. Aufl., 1924, p. 606; also, *Toxikologie*, by Starkenstein, Rost and Pohl, 1929, p. 421; Lewin, *Gifte und Vergiftungen*, 1929, p. 803.

[2] *Lehrbuch der Intoxikationen*, 2te. Aufl., 1906, **2**, 1054.

[3] New York Med. Jour., 1906, **84**, 799.

[4] See Greenway, Brit. Med. Jour., 1878, **2**, 516, in which marked dilation was observed although the autopsy was not made until 64¼ hours after death.

[5] See Brunetiere, Arch. d'anthrop. crim., 1907, **22**, 168; also, McNally, Jour. Amer. Med. Assoc., 1915, **65**, 1640.

Detection.—The stomach and intestinal contents, the blood, urine, and the liver, kidneys, and brain are especially suitable for the detection of these solanaceous alkaloids. In separating these alkaloids from the tissues, the process outlined on page 344 should be followed, special care being taken to prevent hydrolysis. The extractions should be carried out at a relatively low temperature, the extracting fluid being made only slightly acid with tartaric acid, and the alkalinization being done with sodium bicarbonate, or with only a *very slight* amount of ammonium hydroxide. The immiscible solvents may be chloroform, ether, or benzene.

Atropine does not readily decompose in putrefactive tissues, Ipsen[1] isolating it from a cadaver after more than 3 years' burial. Among the products of putrefaction of animal tissue, there may not infrequently be found substances, the so-called "ptomatropines", which resemble, both as to symptoms produced and chemical reactions observed, the atropine group of alkaloids, yet careful analysis will show considerable variation in many of the reactions noted. It is important, however, to remind the analyst that single reactions should never form the basis of an unequivocal report as to the identity of a residue obtained in the extraction processes.

Biologic Tests.—1. *Upon the Eye.*—The eye of man or of a cat may be employed for this test. The human eye is far more sensitive to the action of these alkaloids than is the feline, but, if the test is to be applied to the human eye, somewhat more care must be taken to purify the product. Prepare a solution of the purified residue, obtained in the extraction process, in a *very* dilute sulphuric acid and instill one or two drops of this solution from a pipet into the inner canthus of one eye of a cat, comparing its pupil from time to time with that of the other eye. Feddersen[2] fixes the minimum quantity of atropine sulphate, which will distinctly dilate the pupil of a human adult, at 0.0002 mg., while Führer[3] states that 0.01 mg. causes a slight dilatation of the pupil of a cat, and Autenrieth[4] asserts that 1 drop of an atropine solution 1:130,000 will cause distinct dilatation of the human or cat's eye. This mydriatic effect is shown by all members of this group, the degree of dilatation depending on the dose and time of observation, the enlargement with homatropine appearing somewhat more quickly, being less complete, and passing off sooner than that with atropine. Mydriasis is not, however, sufficient in itself to warrant a conclusion that a certain residue contains a member of this group, as cocaine, ephedrine (the alkaloid of *Ephedra vulgaris*), adrenaline, and ptomatropines produce similar results.

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[1] Vrtljschr. f. ger. Med., 1906, **31**, 308. See, also, Magnette, Jour. pharm. Belg., 1925, **7**, 757, 781, 797, and 821.

[2] *Beitrag zur Atropinvergiftung*, Dissert., Berlin, 1884, p. 37.

[3] *Nachweis und Bestimmung von Giften auf biologischem Wege*, Berlin, 1911, pp. 162 and 165.

[4] *Detection of Poisons and Powerful Drugs*, 6th Amer. Ed., translated by Warren, 1928, p. 180.

2. *Upon the Heart.*—If the heart of a large water-frog be exposed and a few drops of muscarine solution be passed through a canula into the heart or be dropped directly on the heart muscle, a gradual slowing of the cardiac action is observed with final arrest in diastole. If, now, the muscarine be washed out of the heart and a small amount of an aqueous solution of a salt of atropine be added, or if the solution be applied directly to the muscle, the heart will begin to pulsate and soon become quite rapid, due to the paralysis of the terminations of the vagus. According to Harnack[1] 0.0025 mg. of atropine administered to a frog will overcome the effect of muscarine.

Chemical Tests.—1. *Vitali's Test.*—Either the solid alkaloid or any of its salts, with exception of the hydrochloride, may be used in this test. In a small porcelain evaporating dish place a little of the residue obtained in the extraction process, or evaporate a portion of the aqueous solution, add a few drops of fuming nitric acid, and evaporate to dryness on the water-bath. Allow the colorless or, at most, very slightly yellow residue to cool and add a few drops of fresh alcoholic solution of potassium hydroxide. A fine violet color is produced, soon fading to dark red and then disappearing. The color may be made to reappear by adding more alcoholic potash solution. This test is said to be given by 0.001 mg. of atropine. It reacts with all of the solanaceous alkaloids, with exception of homatropine. This reaction of Vitali is fairly characteristic for this group of mydriatic alkaloids, especially if the sequence of colors given above be obtained. Other alkaloids, such as pseudo-aconitine, veratrine, strychnine, apomorphine, physostigmine, and pilocarpine, as well as some ptomatropines, may possibly interfere with or mask the typical Vitali reaction, yet other reactions of this mydriatic group as well as the reactions for the other alkaloids mentioned will easily differentiate them.

2. *Gerrard's Test.*—To a portion of the purified residue, obtained in the extraction processes, add 1 to 2 cc. of a 2 per cent. solution of mercuric chloride in 50 per cent. alcohol, and warm gently. The residue becomes yellow and finally brick-red in color, due to precipitation of mercuric oxide (with a trace of mercurous oxide), if atropine, hyoscyamine, or homatropine be present. No yellow or red precipitate is obtained with scopolamine, owing to its lesser basic character. Gerrard reports white precipitates, which may become slightly yellow on heating with strychnine, brucine, morphine, codeine, veratrine, aconitine, coniine, gelsemine, caffeine, cinchonine, cinchonidine, quinine, and quinidine. According to Flückiger cocaine gives a pure white precipitate, which soon turns red.

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[1] Arch. f. exp. Path. und Pharm., 1874, **2**, 331.

3. *Wormley's Bromine Test.*—An aqueous solution of hydrobromic acid saturated with bromine (Wormley's reagent) produces with atropine or hyoscyamine and their salts, even in such dilutions as 1:10,000, a yellow amorphous precipitate which becomes crystalline in a short time, the crystals being quite characteristic and appearing in bunches of needles or as lanceolate leaf-like crystals grouped together like the petals of a flower. In very dilute solutions the crystals are not so clearly defined. This test may be employed by the micro-method by adding a drop of the reagent to a drop or two of an aqueous solution of the suspected salt on a glass slide and allowing the mixture spontaneously to evaporate somewhat before placing the cover glass on the preparation.[1]

l-Scopolamine produces with this reagent a precipitate of minute brownish globules, which may change to groups of tabular crystals often arranged in leaf-like rosettes, even in dilutions of 1:2000, according to Carr[2], although in some cases the precipitate crystallizes with great difficulty. Indefinite and not characteristic crystals are given, also, by homatropine with Wormley's reagent.

4. *Wasicky's Test.*—If a trace of the suspected residue obtained in the extraction processes be treated with 1 drop of Wasicky's reagent[3] and warmed gently, a red color appears, which becomes an intense cherry-red to violet and remains unchanged for at least 24 hours, in the presence of atropine, hyoscyamine, and scopolamine, but homatropine does not respond to the test.

5. *Gold Chloride Test.*—If there be sufficient material obtained in the extraction processes, the formation and examination of the chlor-aurates of the solanaceous alkaloids yields evidence of some value in the differentiation of the members of this group. In making this test, proceed as follows. Dissolve a little of the suspected residue in dilute hydrochloric acid, and treat this solution with a slight excess of chlor-auric acid, warming the mixture to facilitate solution. Allow the solution to cool, when the chlor-aurate will settle out in a characteristic form, the properties, melting point, and percentage of gold of these precipitates being given under the discussion of the properties of the alkaloids.[4]

Determination.—This estimation may be made either by the volumetric method or by the gravimetric routine. If the former be employed, dissolve the residue obtained in the completed extraction processes in neutralized alcohol, and add a measured amount of N/50 sulphuric acid, followed by a little distilled water. Titrate the excess of acid with N/50 sodium hydroxide, using either cochineal or methyl red as indicators. Each cc. of N/50 acid combined with the alkaloid represents 0.005786 gram of atropine.

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[1] Instead of the Wormley reagent, one may employ a solution of 1 gram of bromine and 2 grams of potassium bromide in 20 cc. of water, as recommended by Eder. See Wagenaar, Pharm. Weekblad., 1928, **65**, 1213 and 1226.

[2] "Atropine and Its Allies" in Allen's *Commercial Organic Analysis*, 1912, **6**, 308.

[3] Dissolve 2 grams of p-dimethyl-amino-benzaldehyde in 6 grams of concentrated sulphuric acid, and carefully add 0.4 gram of water. This combination forms a dark yellow liquid, which keeps for 2 weeks. See, Wasicky, Ztschr. f. anal. Chem., 1915, **54**, 393; also, Jour. pharm. chim., 1917, **15**, 54.

[4] See Wagenaar, Pharm. Weekblad, 1928, **65**, 549.

If one prefers the gravimetric method, dissolve the residue in dilute sulphuric acid and add this to an excess of Wagner's reagent (see page 604), stirring the mixture well and allowing it to stand for a time. Filter, wash with water, dry and weigh as atropine hydriodide octaiodide. If the weight be multiplied by 0.202 the product is the amount of atropine as the free base.[1]

Cocaine and Cocaine Substitutes

Cocaine ($C_{17}H_{21}NO_4$) is the chief alkaloid of the leaf of *Erythroxylon coca*, constituting about 0.75 per cent of the freshly dried leaf. This plant is indigenous in South America, but has been introduced into India, Ceylon, and Java. Besides cocaine, several other alkaloids are found in this leaf, chief among which are hygrine ($C_8H_{15}NO$, isomeric with tropine, but is not a tropane derivative, but, rather, one of pyrrolidine, being known as 1-methyl-2-acetonylpyrrolidine), cinnamyl-cocaine ($C_{19}H_{23}NO_4$), α-truxilline ($(C_{19}H_{23}NO_4)_2$, cocamine, isoatropyl-cocaine), β-truxilline ($(C_{19}H_{23}NO_4)_2$), benzoyl-ecgonine ($C_{16}H_{19}NO_4$), and tropacocaine ($C_{15}H_{19}NO_2$, benzoyl-Ψ-tropeine).[2] Few of these latter alkaloids have any special physiologic or toxicologic value, although all of them, with the exception of hygrine and tropacocaine are derivatives of ecgonine.

The earliest reported case of cocaine poisoning is, apparently, the one of attempted suicide mentioned by Plass.[3] Witthaus[4] has collected 384 cases up to 1909, to which we have been able to add 14 further cases. Of this total of 398 cases, 10 were attempted or actual suicide, none homicidal, the remainder accidental, 76 of them being fatal. Owing to the large increase in the cocaine habit during the years since the War, it is probable that many fatal cases occur annually, which are never reported as such.

Cocaine was first isolated by Niemann from the leaves of peruvian coca. On saponification with water, cocaine splits into methyl alcohol and a base, benzoyl-ecgonine; while the latter base is further hydrolyzed into benzoic acid and ecgonine, if the saponification be conducted with mineral acids or alkalies.

Like tropine (discussed under atropine) ecgonine belongs to the tropane-ring system and differs from tropine only in the replacement of a hydrogen atom of the second atomic group by a carboxyl group. Ecgonine may be, therefore, represented graphically as follows, while cocaine, being the methyl-benzoyl ester of ecgonine shows the following structure:

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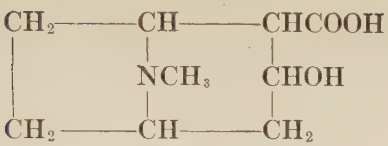
[1] See Prescott and Gordin, Jour. Amer. Chem. Soc., 1898, **20**, 329, 712, 722, and 724.

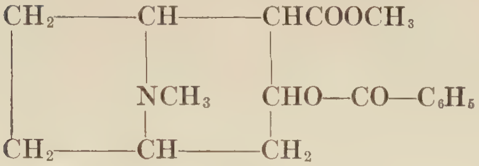
[2] For properties of these less important alkaloids see Schmidt, "Pflanzenalkaloide" in Abderhalden's *Biochemisches Handlexikon*, 1911, **5**, 93 *et seq.* and *Chemistry and Analysis of Drugs and Medicines* by Fuller, 1920, p. 118 *et seq.*

[3] Ztschr. f. Med. Chir., und Geburtsh., 1863, N. F., **2**, 222.

[4] *Toxicology*, 1911, 897.



Ecgonine



Cocaine

Corresponding to the different stereoisomeric ecgonines, cocaine exists in three forms, l-cocaine, d-cocaine, r-cocaine, while a fourth cocaine, known as α-cocaine, has the carboxymethyl and the benzoylhydroxyl groups attached to the same carbon atom. The optical activity of these cocaines rests in the basic part of the molecule, while that of the atropine group is resident in the acid portion. l-Cocaine seems to be the only one of these cocaines possessed of medicinal value.

Properties.—l-Cocaine occurs in large, colorless, 4 or 6-sided monoclinic prisms or as an odorless, white, crystalline powder, stable in the air, and melting between 96° and 98°C. One gram dissolves in about 600 cc. of water, 6.5 cc. of alcohol, 0.7 cc. of chloroform, 3.5 cc. of ether, 12 cc. of olive oil, and in 30 to 50 cc. of liquid petrolatum at 25°C. One gram is soluble in 270 cc. of water at 80°C. It is very soluble in warm alcohol. Insoluble in glycerin. Cocaine is levorotatory, its specific rotation in chloroform solution being about $-15.8°$ for the sodium ray. Its solutions are alkaline to litmus, cochineal, iodeosin, and methyl orange, but not to phenolphthalein. It is precipitated by the general alkaloidal reagents, its chloraurate melting at 198°C., while its chlorplatinate melts at 122.5°C. to 123°C.

The official *Cocaine hydrochloride* ($C_{17}H_{21}NO_4HCl$) occurs in colorless, transparent, monoclinic prisms; in flaky, lustrous leaflets; or as a white crystalline powder. It is odorless, permanent in the air, and melts between 183° and 191°C., the higher the melting point the greater the purity of the salt. One gram of the hydrochloride dissolves in 0.4 cc. of water, 3.2 cc. of alcohol, and in 12.5 cc. of chloroform at 25°C. One gram is soluble in 2 cc. of alcohol at 60°C. It is soluble in glycerin and insoluble in ether. Its aqueous solutions are neutral and levorotatory. As a special test of purity of the official salt, the MacLagan test is of some value. In performing this test, proceed as follows: Dilute 5 cc. of an aqueous solution of the salt (1 in 50) with 80 cc. of distilled water, add 0.2 cc. of 10 per cent. ammonia water, and stir the solution vigorously during 5 minutes, occasionally rubbing the sides of the beaker with a stirring rod. A crystalline precipitate of cocaine forms at the bottom and the supernatant liquid is clear. The presence of 0.5 per cent. of allied coca bases (especially α-truxilline, isoatropyl-cocaine) will prevent the formation of nearly all of the precipitate and will cause the supernatant liquid to be milky.[1]

Symptoms.—The symptoms of cocaine poisoning usually appear promptly, progress rapidly, and are ordinarily over within 2 to 3 hours. The longer the continuation of the toxic symptoms, the better the outlook for recovery. The symptoms noted after intake of cocaine are the result of a primary stimulation followed by a depression of the central nervous system, the characteristic action being a local paralyzing effect. "The action of cocaine on the central nervous system is primarily a descending stimulation, the cerebrum being first affected, then the hind brain and medulla oblongata, and, last of all, the spinal cord. Perhaps it might be better expressed by saying that after small quantities the chief symptoms arise from the cerebrum, but as the dose is increased those from the lower parts of the central axis tend to become more prominent. After the stimulation there succeeds depression, which follows the stimulation downward, affecting first the cerebrum and then the lower divisions. The two stages are not definitely divided, however, one part of the cerebrum often showing distinct depression, while another is still in a condition of excessive activity. In some cases, especially in man, when a large dose is rapidly absorbed, the stage of excitement may be very short or apparently absent and the whole course of the symptoms then points to medullary depression."[2] Cocaine also paralyzes the terminations of the sensory nerves, and tends to decrease the secretions, although there is some variation in this action.

If a poisonous dose be taken by the mouth, hypodermically, or by absorption through an abraded surface or a portion of the mucous membrane, severe symptoms quickly appear, varying considerably in different individuals. In most cases there is excitement, pleasurable or disagreeable. The patient is generally restless and more talkative than usual, the speech being incoherent or foolish. Not infrequently the mental disturbance may progress to delirium with hallucinations, or may lead to a violent maniacal condition. Occasionally, however, there may be a calmness with little tendency to sleep, the patient being fully conscious of what is going on around him. There may be a feeling of dryness in the mouth, nose, and throat, difficulty in swallowing, and a feeling of suffocation. Nausea is an early symptom, although vomiting is by no means common, and a burning pain in the stomach may be prominent. There may be vertigo or severe pain and burning sensations in the head. Numbness, tingling, or prickling of the hands and feet, or an anesthesia at the point of application of the drug may be noted. Pulse is accelerated and feeble at first, although the heart may be bounding and tumultuous.

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[1] See U. S. Pharmacopoeia, 10th Rev., 1925, p. 113; and Breteau, Jour. pharm. chim., 1928, **7**, 329; Abstract in Chemical Abstracts, 1928, **22**, 3263.

[2] Cushny, *Pharmacology and Therapeutics*, 9th ed., revised by Edmunds & Gunn, 1928, 374.

Later the heart becomes slow, weak, and irregular. Respirations are at first quick and deep, gasping, or even of Cheyne-Stokes' type; later this becomes slow and shallow, with intermittent periods, with final arrest. Pupils are generally dilated and insensible to light, although they may, rarely, be normal or even contracted, the eyes usually being protuberant and showing paralysis of accommodation. Reflexes are usually somewhat more easily excited than usual, and tremors or slight convulsions may occur. Later powerful tonic or clonic convulsions appear, although, in some cases, convulsions are absent, and periods of unconsciousness are noted. Roberts[1] calls attention to the occurrence of tetany following the use of cocaine and epinephrine in internasal operations. The skin is pale and cold in the early stages, and covered with a free perspiration, but occasionally the skin may be dry. Death results from gradual respiratory failure, this invariably preceding cardiac failure. Recovery may be rapid and complete, or extreme prostration may continue for some time.

Chronic poisoning, with which may be classed the effects of the cocaine habit or addiction (*cocaineismus*), is more a problem of the physician than of the toxicologist. Contrary to the usual view, Tatum[2] believes that human beings can not continue taking cocaine indefinitely, nor can a tolerance to this drug be built up. In contradistinction to morphine, Tatum finds that cocaine may be taken away from an habitue with no more disastrous effect than taking tobacco away from a confirmed smoker. Tatum has shown, also, that experimental animals may develop the psychoses so characteristic of the effects of this drug upon human beings. Fatal poisoning has occurred in an addict.[3]

Fatal Dose.—It is a difficult matter to state definitely the lethal dose of cocaine, owing to the variable susceptibility of different individuals, and, also, to the fact that the cases reported in the literature do not always give the quantity taken or the strength of solution used. The presence of adrenaline seems to increase the toxicity of cocaine.[4] In considering the question of the fatal dose the portal of entry of the drug must be regarded as of great importance. While Mannheim[5] considers 1 gram as the lethal dose, whether given by mouth or parenterally, and Kunkel[6] states this as something over 1.2 grams, many cases are reported in which larger amounts have not caused death, and, on the other hand, smaller doses have proven fatal. Thus, 0.02 gram administered by subdural injection has caused death in 2 cases[7]; 0.03 gram (0.46 grain) per urethra[8]; 0.04 gram given subconjunctivally[9]; 0.2 to 0.3 gram by subcutaneous injection[1]; 0.648 gram (10 grains) per os[2]; and 1.5 grams per rectum.[3] Cloetta[4] states that concentrated solutions are more toxic than dilute ones, although the same amount of cocaine be injected.

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[1] Jour. Amer. Med. Assoc., 1929, **93**, 905.

[2] Science, 1925, N. S. **61**, XIV.

[3] See Mancini, Riv. Crit. di Clin. Med., 1922, **23**, 121.

[4] See Ross, Jour. Lab. and Clin. Med., 1923, **8**, 656.

[5] Ztschr. f. klin. Med., 1890, **16**, 380.

[6] Cited by Kobert, *Lehrbuch der Intoxikationen*, 2te. Aufl., 1906, **2**, 1018.

[7] Legueu, Cited by Kobert, *Loc. cit.*, 1019.

[8] Haynes, Med. News, 1894, **65**, 144.

[9] Abadie, Internat. klin. Rundschau, 1888, **2**, 1746.

Fatal Period.—In acute poisoning by cocaine the symptoms appear quickly after the absorption of the poison, and run a rapid course. According to Witthaus[5] in 5 of 37 cases in which the duration is recorded, death occurred "immediately" or "soon", and in 6 in 2, 3, 5, or "a few" minutes. Rarely is life prolonged more than 3 hours. Haines[6] states that, generally, if the patient survives ½ hour, he recovers.

Treatment.—If the poison has been taken by mouth, gastric lavage should be performed at once, finely powdered charcoal being added to the lavage water. If the poison has been ingested parenterally, or after toxic symptoms are manifest from administration per os, stimulants should be administered to combat the symptoms of collapse. Artificial respiration may be necessary to overcome the respiratory depression, which is so marked in this type of poisoning. Depressing agents, such as chloral, chloroform, and, especially, morphine have been used, but are more properly contraindicated. Hofvendahl[7] and Tatum and his colleagues[8] have found that administration of soluble barbituric hypnotics relieves the convulsions and the general symptoms of cocaine poisoning in animals, barbital sodium alone or a mixture of this compound with paraldehyde being used in both prophylaxis and treatment. Guttman[9] advises the giving, as a prophylactic, of 0.2 gram of phenobarbital by mouth 30 minutes before operation at which cocaine is to be employed. In cases of mild intoxication, he administers hypodermically 0.2 gram of barbital sodium dissolved in sterile saline solution, or, as advised by Tatum, 5 cc. of a saturated solution of paraldehyde containing 100 mg. of barbital sodium per kilogram of weight, this mixture being used intravenously if the case be severe. The results are good. The use of calcium chloride, as advised by Mayer[10], seems to be of little value in controlling cocaine poisoning.

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[1] Starkenstein, Rost and Pohl, *Toxikologie,* 1929, p. 411.

[2] Curgenven, Quart. Med. Jour., 1895, **4,** 152.

[3] Szuman, Therap. Monatsh., 1888, **2,** 393.

[4] "Die Vergiftungen durch Alkaloide und Pflanzenstoffe" in *Lehrbuch der Toxikologie* by Flury and Zangger, 1928, p. 285.

[5] *Toxicology,* 1911, p. 902.

[6] Hamilton's *System of Legal Medicine,* 1894, **1,** 428.

[7] Monatschr. f. Ohrenh., 1921, **55,** 887; Ztschr. f. Hals-, Nasen-und Ohrenh., 1922, **1,** 233.

[8] Tatum, Atkinson, and Collins, Jour. Amer. Med. Assoc., 1925, **84,** 1177; Jour. Pharm. and Exp. Therap., 1925, **26,** 325; Tatum and Collins, Arch. Int. Med., 1926, **38,** 405. See, also, La Mendola, Arch. farm. sper., 1924, **37,** 256.

[9] Jour. Amer. Med. Assoc., 1928, **90,** 753; and Ill. Med. Jour., 1929, **56,** 59. See, also, Martin, Ibid., 1928, **91,** 555.

[10] Mayer, Ztschr. f. Ohrenh., 1922, **82,** 42. See, also, Fabry, Münch. med. Wchnschr., 1922, **69,** 969; Frank, Strauss, and Smiley, Jour. Amer. Med. Assoc., 1923, **80,** 1908; Weiss, Ibid., 1923, **81,** 1282.

Postmortem Appearances.—There are no postmortem findings which are at all characteristic of cocaine poisoning. The liver, kidneys, spleen, lungs, brain, and meninges are markedly congested, while the mucous membrane of the stomach may show slight hyperemia.

Detection.—Cocaine is absorbed quite readily in whatever manner it may be administered, larger amounts being absorbed where concentrated solutions are employed than when dilute solutions are used, even though the exact amount of the alkaloid in each of the solutions be the same. Cocaine, as stated above, is somewhat readily saponified, so that failure to detect it in forensic cases has been attributed to such decomposition by the tissues of the body, Sonnie-Moret[1], for instance, asserting that toxicologic examination will give negative results unless cocaine be taken in considerable quantities. While Wiechowski[2] found that only 5–12 per cent. of the intake of cocaine was excreted in the urine of dogs, Rifàtwachdani[3] showed that, in rabbits, prolonged contact with living tissue does not, apparently, cause destruction of cocaine, 42 per cent. to 85 per cent. of the intake appearing in the urine and cocaine being detected in the tissues. It is questionable as to just how rapidly cocaine may be decomposed in the system, although Proells[4] states that he was able to detect cocaine in cadaveric material at most after 14 days, and Popp[5] was unable to establish the presence of cocaine in the organs received 5 days after death. While cocaine belongs to the group of poisons which are detectable in the cadaver only relatively soon after death, yet, if the methoxyl and benzoyl groups are so easily split off as claimed, it should be possible to detect ecgonine in the urine and tissues by the method advised by Rifàtwachdani.[6]

The method of extraction of cocaine from the tissues is the same as that given for atropine (p. 637). Instead of chloroform, benzene should, preferably, be used as the immiscible solvent.

The tests for cocaine are neither especially delicate nor characteristic, although one may be quite certain of his results, if both biologic and chemical tests prove positive. It should be insisted upon that no single test is sufficient for identification of any alkaloid, especially of cocaine.

Biologic Tests.—Dissolve a small amount of the residue obtained in the extraction processes in a few drops of dilute hydrochloric acid and evaporate to dryness on the water-bath. Dissolve the residue (which should be neutral in reaction) in a little distilled water, and apply a drop of this solution to the tongue by means of a glass rod, repeating the contact upon the same spot. If cocaine be present, a sense of numbness and a characteristic insensibility to touch (anesthesia) will be noted, this sensation lasting but a few minutes unless the application be repeated. If a few drops of the above solution be applied to the eye of a frog or of a cat, the anesthetic and blanching effects upon the conjunctiva are obtained, and, in addition, a dilatation and fixedness of the pupil are observed, the latter effect being less extreme and less persistent than that noted after the application of atropine. If some of the above solution be injected hypodermically, anesthesia at the point of application will be observed after a few minutes, unless the solution be excessively dilute.

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[1] Jour. de pharm. et de chim., 1893, **28**, 390; Chem. Centralbl., 1893, **1**, 859.

[2] Arch. f. exper. Path. und Pharm., 1901, **46**, 155. See, also, Kohlhardt, Arch. f. klin. Chir., 1902, **64**, 927.

[3] Biochem. Ztschr., 1913, **54**, 83.

[4] Apotheker-Zeitung, 1901, **16**, 288, 306, 325, 779, and 788.

[5] Chemiker-Zeitung, 1922.

[6] Biochem. Ztschr., 1913, **54**, 83.

Chemical Tests.—Many chemical tests have been advocated for the detection of cocaine, but few of them are applicable to forensic work, as the amount of material required is, usually, larger than that at the disposal of the analyst. We give those that seem to promise the best results in toxicological examinations.

1. *Guerbet's Test for Benzoic Acid.*[1]—To 0.1 mg. or more of the alkaloidal residue obtained in the extraction processes add 3 to 4 drops of fuming nitric acid and evaporate to dryness. Take up the mixed nitro compounds with 1 drop of a 10 per cent. solution of stannous chloride[2], heat for 2 or 3 minutes, cool, and add 2 drops of a 1 per cent. solution of sodium nitrite and 3 or 4 drops of a 1 per cent. solution of β-naphthol in 10 per cent. ammonium hydroxide. A deep orange-red precipitate is formed in the presence of benzoic acid. If this precipitate be dried and dissolved in 1 cc. of concentrated sulphuric acid, a violet-red solution is obtained which, on pouring into water, changes to a brilliant yellow color, still visible with 0.01 mg. of benzoic acid. This test is of value only in showing the presence of benzoic acid in the material examined, or in its splitting products, and can not, of course, be taken as proving the presence of cocaine, although a negative test shows that this alkaloid is not present.

2. *Iodic Acid Test.*—This test is, also, one traceable to the splitting off of benzoic acid from cocaine.[3] To a trace of the residue obtained by extraction add a few drops of concentrated sulphuric acid and a small particle of pure potassium iodate or of pure iodic acid. No color appears in the cold. If, now, this mixture be heated in a small porcelain dish over a small flame, until the vapors of sulphuric acid come off, or even a little longer, then appear in succession and along with one another brown, olive-green, blue, and violet shades of color, and, finally, iodine vapors develop. This test will detect 0.05 mg. of cocaine. Most other alkaloids give intense colorations with sulphuric acid and potassium iodate, but these colors appear in the cold. Ecgonine, under the conditions of the test, gives cherry to purple-red, and, finally, dirty violet shades.

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[1] Jour. de pharm. et de chim., 1920, **22**, 321.

[2] Guigues (Bull. sci. pharmacol., 1928, **35**, 292; Chem. Abs., 1928, **22**, 3019) recommends that this be freshly prepared by dissolving pure tin in HCl, and evaporating twice to dryness on the water-bath, when a salt is obtained completely soluble in water.

[3] See Gadamer, *Lehrbuch der chemischen Toxikologie*, 2te. Aufl., 1924, p. 567.

3. *Seiter's Test.*—This test[1] is a modification of that of Giesel[2]. To 1 cc. of an aqueous cocaine solution, obtained in the extraction processes, add 1 drop of 25 per cent. sulphuric acid and 1 cc. of a saturated (about 7½ per cent.) potassium permanganate solution. After standing for sometime, a drop of the liquid is removed to a glass slide, the cover-glass adjusted, excess of liquid removed, and a drop of water drawn under the cover-glass by means of a piece of filter-paper placed on the opposite edge. On examining the slide under the microscope, characteristic translucent, violet-red rhombic (almost rectangular) plates of cocaine permanganate are noted, which crystals are often grouped to form rosettes.

4. *Metzger's Test.*—On adding a few drops of a 5 per cent. solution of chromium trioxide (chromic acid) or a 7.5 per cent. solution of potassium dichromate to an aqueous solution of cocaine hydrochloride, a yellow precipitate is produced, which redissolves on shaking the mixture. Now add to the clear solution about 1 cc. of concentrated hydrochloric acid, when an orange-colored precipitate of fine needles is obtained. This reaction is shown in solutions of a strength of 1:1000 and is not given, according to Metzger,[3] by any of the other common alkaloids.

5. *Gold Chloride Test.*—A solution of cocaine hydrochloride, which may be prepared by careful treatment of a film of residue of the free alkaloid from the extraction processes with a drop or two of very dilute HCl, is at once precipitated by gold chloride, if the solution be as strong as 1:3000. Under the microscope stellate crystals are noted, resembling fern fronds, and melting at 198°C. If the test be done as a micro-chemical test, as advocated by Denigès[4], crystals may be obtained from solutions as dilute as 1:12000.

COCAINE SUBSTITUTES

A large number of synthetic products have been introduced as local anesthetics and substitutes for cocaine in the attempt to obtain a more stable product having the local effects of cocaine, but without its toxic power. Although some of these substitutes do have a lower degree of toxicity, yet some of them are distinctly more toxic than cocaine, and practically all of them have produced untoward symptoms, while some of them have caused death. These products react, in a general way, like alkaloids, yielding precipitates with most of the alkaloidal reagents and showing somewhat characteristic chemical reactions by which they may be identified, yet their isolation and detection in actual cases of poisoning have not been extensively investigated. As far as we have found, the literature does not reveal the record of a single successful toxicologic investigation of a case of poisoning by any of these substitutes, the cause of death having been determined largely from the history of administration of some local anesthetic and the more or less prompt appearance of toxic symptoms.

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[1] Amer. Jour. Pharm., 1911, **83**, 265; also, Seiter and Enger, Ibid., 195.

[2] Pharm. Zeit., 1886, **31**, 132.

[3] Pharm. Zeit., 1889, **34**, 697.

[4] Ann. chim. anal. chim. appl., 1919, **1**, 65.

The most important of these cocaine substitutes owe their origin to the discovery that the local anesthetic action of cocaine is due to the benzoic acid radical in combination with a nitrogen-containing basic group. The simplest of these compounds, anesthesine (benzocaine, now official under the name of *Aethylis Aminobenzoas*), propaesine, butesin, and cycloform, are respectively the ethyl, propyl, n-butyl, and iso-butyl esters of para-amino-benzoic acid ($C_6H_4NH_2COOH$); while orthoform (orthoform-new) is the methyl ester of meta-amino-para-oxy-benzoic acid ($C_6H_3OHNH_2COOH$). All of these are too weak or too insoluble in water to be useful for hypodermic injection, but may be employed as local applications, and may be regarded as only slightly toxic.

Besides the above simple cocaine substitutes, others of a somewhat more complex structure and, at the same time, more soluble and more toxic, have from time to time found more or less use in medical practice, although many of these have now been discarded owing to their high toxicity. Practically all of these substitutes differ from cocaine in dilating the vessels, or, at least, in not constricting them as does cocaine. For this reason it is customary to employ epinephrine (adrenaline) in conjunction with them, but it must be remembered that this latter basic substance may, also, prove toxic. Among these more complicated cocaine substitutes we find α-eucaine ($C_{19}H_{27}NO_4HCl$, the hydrochloride of the methyl ester of α-α'-tetramethyl-n-methyl-γ-benzoyl-oxypiperidine-γ-carboxylic acid), β-eucaine (the official hydrochloride having the formula $C_{15}H_{21}NO_2HCl$, and being 2, 6, 6-trimethyl-4-benzoyl-oxypiperidine hydrochloride), butyn ($C_{18}H_{30}N_2O_2H_2SO_4$, the sulphate of p-aminobenzoyl-γ-dinormalbutylaminoproponol), alypin, $C_{16}H_{26}NO_2HCl$, the hydrochloride of 2-benzoxy-2-dimethyl-aminomethyl-l-dimethylaminobutane), tutocaine (butamine,$C_{14}H_{22}N_2O_2HCl$, the hydrochloride of p-amino-benzoyldimethyl-amino-methyl-butanol), apothesine $C_{16}H_{23}NO_2HCl$, the hydrochloride of γ-diethyl-aminopropyl-cinnamate), procaine (novocaine, official as the hydrochloride $C_{13}H_{20}N_2O_2HCl$, l-para-amino-benzoyl, 2-diethylamino ethane), phenacaine (holocaine, $C_{18}H_{22}N_2O_2HCl$, the hydrochloride of ethenyl-p-diethoxydiphenyl-amidine), stovaine ($C_{14}H_{21}NO_2HCl$, the hydrochloride of the dimethylamino-ethyl-isopropyl ester of benzoic acid), tropacocaine ($C_{15}H_{19}NO_2HCl$, the hydrochloride of benzoyl-Ψ-tropeine), and psicaine ($C_{21}H_{27}NO_{10}$, the acid tartrate of dextro-Ψ-cocaine).

The above local anesthetics have been employed at various times, but some of them, at least, have been discarded as too toxic for general use. In a large series of experiments Copeland[1] found that the best of the local anesthetics for the eye are cocaine and butyn; tutocaine may also have a use here; tropacocaine, novocaine, and eucaine are less valuable for deep anesthesia; for the nose, cocaine and tutocaine are alone useful; while for subcutaneous injection novocaine is much the best. Psicaine has been found to have about twice the activity of cocaine when brought in contact with peripheral nerve endings, and its use is especially indicated in superficial anesthesia, especially upon mucous surfaces.[1]

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[1] Brit. Med. Jour., 1924, **2**, 41.

In an investigation by a committee of the American Medical Association on the "Toxic Effects Following the Use of Local Anesthetics"[2], 43 deaths were reported which had not found their way into the literature, of which 1 was due to alypin, 4 to apothesine, 4 to butyn, 1 to butyn and cocaine, 26 to cocaine (alone and with procaine), 2 to procaine, 1 to stovaine, 2 to unclassified cause, and 2 to causes other than local anesthetics. The Committee states that such accidents are more frequent than is commonly supposed; that accidents occur with the more recently introduced synthetic anesthetics as well as with the older agents; that dyspnea and the arrest of respiration within a few minutes after the administration are especially characteristic; so much so that it is questionable whether later deaths can be charged to anesthetics; that in the treatment of accidents, the first place must be assigned to artificial respiration, perhaps with cardiac massage; and that the committee advises strongly against the routine use of morphine and epinephrine in the treatment of accidents. In a supplementary paper, Mayer[3] reports on 14 additional deaths, 3 from cocaine, 2 from cocaine-procaine, 8 from cocaine, and 1 from butyn. To these cases may be added 1 from alypin reported by Riley[4], 2 from procaine 1 cited by Martin[5] and 1 reported by Snapp[5], and 1 from butyn reported by Jamieson[6]. Recently Klotz[7] tabulated 151 cases, of which 102 deaths were due to cocaine alone or with other local anesthetics. He states that fatal accidents are relatively few in view of the frequency with which these local anesthetics are employed, and that accidents are due mainly to overdosage, to injections of cocaine, to the use of solutions of too high concentrations, to excessive doses of epinephrine, and a smaller number to peculiar conditions of the patient which are beyond evaluation by the physician.[8]

In the handling of these toxic cases it is probable that the routine use of soluble barbital preparations will control the dangerous symptomatology[1]. Many of these cases are, undoubtedly, due to idiosyncrasy, so that great care must be taken to obtain a history of possible toxic actions previously shown by the patient, if such be possible, before giving any of these local anesthetics. In this connection it is interesting to find that the courts have ruled that death from "idiosyncrasy" to procaine is an accidental death and was caused by accidental means.[2]

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[1] See Copeland, Ibid., 1925, **1**, 9; and Watson-Williams, Ibid., 11.

[2] Mayer, Jour. Amer. Med. Assoc., 1924, **82**, 876. See, also, Report of the Committee on the Advantages and Disadvantages of the Various Local Anesthetics in Nose and Throat Work, Trans. Sect. Laryng., Otol. and Rhin., A. M. A., 1920, p. 210.

[3] Jour. Amer. Med. Assoc., 1928, **90**, 1290.

[4] New England Jour. Med., 1928, **199**, 267.

[5] Jour. Amer. Med. Assoc., 1928, **91**, 555; Snapp, Anu. of Otol., 1928, **37**, 974.

[6] Jour. Amer. Med. Assoc., 1929, **92**, 1519.

[7] *Les accidents mortels de l'anesthésie locale*, Paris, 1929.

[8] See Editorial, Jour. Amer. Med. Assoc., 1929, **92**, 1680.

The chemical properties of these cocaine substitutes are such that each of them may be detected, when solutions are offered for analysis. As far as their detection in a body after death is concerned, it must be said that the same difficulties arise as in the case of cocaine. If the examinations are made soon after death, it may be possible to extract these basic substances from the organs, especially the liver, but, in the cases reported in which this has been attempted, the results have been negative. For the methods of differentiation and the properties of these compounds I must refer elsewhere.[3]

COLCHICINE

This alkaloid is the distinctive chemical constituent of *Colchicum autumnale*, the meadow saffron. The closely related alkaloid, colchiceine, is much less active than is colchicine, and is present in very small amount in the plant. Colchicine is found in all parts of the crude plant, but chiefly in the seeds and root, both of which serve as the basis of the pharmacopoeial preparations, the extract being derived from the root, while the fluidextract and tincture are prepared from the seed. The dried root of colchicum should yield, according to the Pharmacopoeia, not less than 0.35 per cent. of colchicine; the dried seeds not less than 0.45 per cent; the extract not less than 1.25 nor more than 1.55 per cent; the fluidextract not less than 0.36 nor more than 0.44 per cent; and the tincture not less than 0.036 nor more than 0.044 per cent. The pure alkaloid is official with an average dose of 0.5 mg. ($\frac{1}{120}$ grain).

Cases of poisoning by colchicum and its preparations have been relatively numerous. The literature reveals 9 cases of poisoning with colchicine, 7 of which were fatal. Of 132 reports of poisoning with preparations of colchicum, 118 were accidental, 6 suicidal, and 8 homicidal, the most interesting of these last 8 cases being that of Catherine Wilson, who was tried for the murder of 4 persons with colchicum seeds placed in wine.[4] In accidental poisonings, the leaves have been eaten by mistake for salad, while the seeds have been eaten by children.

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[1] See Hofvendahl, Monatsschr. f. Ohrenhkde., 1921, **55**, 887; Tatum, Atkinson, and Collins, Jour. Amer. Med. Assoc., 1925, **84**, 1177; Jour. Pharm. and Exp. Therap., 1925. **26**, 325; Tatum and Collins, Arch. Int. Med., 1926, **38**, 405; Martin, Jour. Amer. Med, Assoc., 1928, **91**, 555.

[2] See Mutual Life Ins. Co. *v.* Dodge (U. S.), 11 Fed. R. (2d). 486.

[3] See Gadamer, *Lehrbuch der chemischen Toxikologie*, 2te. Aufl., 1924, p. 569 *et seq.*; Autenrieth, *Detection of Poisons*, 6th Amer. Ed. translated by Warren, 1928, p. 387; *New and Nonofficial Remedies*, 1928, p. 53 *et seq.*

[4] See Taylor, *Principles and Practice of Med. Jurisp.*, 6th ed., 1910, **2**, 703.

Properties.—When boiled with acidulated water, colchicine undergoes hydrolysis, splitting into methyl alcohol and colchiceine, this latter alkaloid being converted, by longer boiling, into acetic acid and trimethylcolchicinic acid, according to Zeisel[1], although later studies by Windaus and Schiele[2] show that this latter splitting product contains an aldehyde group and not an acid group, colchicine being, therefore, the methyl ester of this enol-form.

Colchicine ($C_{22}H_{25}NO_6$) occurs in pale-yellow amorphous scales or as a pale-yellow amorphous powder, turning darker on exposure to light; it is odorless, or, if moist and slightly warmed, has an odor resembling hay; and melts between 142° and 146°C. One gram of colchicine dissolves in 22 cc. of water, 220 cc. of ether, and 100 cc. of benzene at 25°C.; also in 21 cc. of water at 80°C.; freely soluble in alcohol, chloroform, and amyl alcohol, but insoluble in petroleum ether. Its aqueous solution is yellow in color (intensified by addition of inorganic acids), is intensely bitter, is neutral in reaction to litmus, and is levorotatory. Its basic characters are very slight, so that it may be extracted from both acid and alkaline solutions. Colchicine is precipitated from its neutral aqueous solutions by such alkaloidal precipitants as tannic acid, Sonnenschein's, Wagner's and Dragendorff's reagents, but yields precipitates with Mayer's reagent only in acid solutions.

Colchiceine ($C_{21}H_{23}NO_6.\frac{1}{2}H_2O$), when crystallized from water, forms lustrous white needles, melting 139° to 141°C., while the anhydrous form melts at 172°C. It is very slightly soluble in cold water, more readily in hot water, dissolves easily in alcohol, chloroform, and amyl alcohol, but is almost insoluble in ether and benzene. Its aqueous solutions possess both acid and feebly basic properties, and are levorotatory. With many of the alkaloidal reagents it yields precipitates which are indistinguishable from those with colchicine.

Symptoms.—The symptoms of poisoning with colchicum and its preparations resemble those of an irritant, such as arsenic or a bacterial toxin. Quite characteristic is the delay in onset of the symptoms, these not appearing before 3 to 5 hours after intake of the poison, so that the assumption has been made that the colchicine is converted by slow oxidation into an active product, oxydicolchicine, $(C_{22}H_{25}NO_6)_2O$. Among the symptoms in most cases are a burning sensation in the throat, nausea, vomiting, severe colicky pains, great thirst, frequent purging, various derangements of the urinary excretion (especially anuria, albuminuria, and hematuria), coldness and moisture of the skin, and prostration of the strength. The pulse is small and irregular, later becoming imperceptible. Respiration gradually becomes shallow, death being due to paralysis of the respiratory center. The blood picture may show a leucocytosis with myelocytes and even nucleated red cells, a basophilia occasionally resulting after repeated injections. The mind is not directly affected, although there may be some confusion or even delirium, vertigo, depression, apathy, and collapse.

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[1] Monatsh. f. Chemie, 1883, **4**, 162; 1886, **7**, 557; and 1888, **9**, 1 and 865.

[2] Liebig's Ann. der Chemie, 1924, **439**, 59.

Fatal Dose.—Of the pure alkaloid, colchicine, 20 mg. may be accepted as a lethal dose, although 4 reports of death from 3 mg. are found in the literature.[1]

Fatal Period.—Following a fatal dose of colchicine, death has occurred in 12 to 31 hours, 3 of the cases arising from a dosage of 3 mg. dying in 12, 21 and 26 hours respectively, while a fourth, with the same dosage, lingered for 10 days. In 58 of 78 fatal cases of which the duration is reported, death occurred, according to Witthaus[2], in less than 48 hours; in 13 cases in from 2 to 7 days, and in 7 after an illness of longer duration. The most rapidly fatal case appears to be that cited by Taylor[3] of death in 7 hours from the effects of 1½ ounces of the wine of colchicum. In some cases, on the other hand, death has been delayed for several weeks.

Treatment.—The stomach and intestines should be washed out as soon as possible with water containing tannic acid, in order to prevent absorption. The mucous irritation may be allayed by mucilaginous drinks and opiates, the abdominal pains are relieved by hot fomentations. To increase the excretion of colchicine by the kidneys, copious quantities of water should be given. Collapse may be combated by strychnine and atropine, while respiratory failure may require artificial respiration.

Postmortem Appearances.—The autopsy findings are not characteristic. The alimentary tract shows evidences of acute gastro-enteritis, with numerous hemorrhagic areas especially in the upper part of the bowel. The kidneys may show marked congestion, and, occasionally, evidence of a toxic nephritis.

Detection.—Colchicine is to be looked for in the vomitus, gastric and intestinal contents, blood, urine, and in the kidneys, while the liver may yield its quota. This alkaloid is readily saponified by heating with dilute acids or alkalies, so that the extraction process must be conducted with care, using room temperature, or, at least, one not over 50°C. To purify the yellowish amorphous product obtained in the extraction processes, follow the method of Autenrieth[4]. Extract the yellowish residue with warm water. Filter the solution, and when cold extract it first with petroleum ether to remove fatty and resinous matter and follow this with chloroform. Or, preferably, precipitate the colchicine from its aqueous solution with tannic acid. Collect this precipitate upon a filter and wash with cold water. Mix the moist precipitate with freshly precipitated and washed lead hydroxide. Dry this mixture, grind to a powder, and extract with chloroform. Evaporation of the solvent leaves nearly pure colchicine, as a yellow varnish-like mass.

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[1] See Klin.-Ther. Wchnschr., 1900, **7**, 407; and Courtois-Suffit et Trastour, Bull. et mém. Soc. des hôp. de Paris, 1903, **20**, 254.

[2] *Toxicology*, 1911, p. 914.

[3] *On Poisons*, 3rd. Amer. Ed., 1875, p. 491.

[4] *Detection of Poisons*, 6th Amer. Ed., 1928, p. 118.

Colchicine resists putrefaction fairly well, so that it may be recovered from the body several months after death. In such cases the possible presence of putrefactive products must be borne in mind. In a few medicolegal cases the tests for colchicine have been brought into question. While it is true that these tests may be simulated by such basic putrefactive products (ptomaines), yet none of these so far discovered have given reactions similar in every detail to those to be mentioned as given by colchicine. In such cases one must insist upon *identity* of color or precipitation reactions and biologic tests, before he gives an unequivocal opinion as to the identity of any residue. To show the possibility of confusion in such cases we cite one case, which put the analysts on their guard, even though the reputed reactions obtained with the putrefactive products were, in reality, not those of colchicine. In the Affaire R[1] Brouardel, Ogier, and Pouchet apparently isolated a basic compound which fully agreed with colchicine in all reactions, the symptoms and postmortem findings also indicating this poison. Schutzenberger and Vulpian, testifying for the defendant, claimed to have isolated from 2 cadavers, in which possibility of poisoning by colchicine was precluded, a basic substance which coincided in its reactions with the base isolated from the suspected organs, showing reactions which were very similar though not identical with colchicine. In view of these findings, the experts for the prosecution would go no further than to state, "Symptoms, autopsy, and chemical analysis are in accord with the view that death resulted from colchicine, but we would not affirm scientifically with absolute certitude, that this hypothesis was correct."[2]

Chemical Tests.—1. *Nitric Acid Reaction.*—The suspected residue treated with concentrated nitric acid gives a violet-red color, changing to green and then to yellow. On addition of strong potassium hydroxide solution, the color is changed to orange-red, if colchicine, colchiceine, or oxydicolchicine be present.

2. *Sulphuric Acid Reaction.*—If the suspected residue be treated with concentrated sulphuric acid, an intensely yellow (lemon) color is produced. If, now, a drop of concentrated nitric acid or a particle of potassium nitrate be added, a play of colors is observed, the yellow changing to greenish-yellow, green bluish-green, wine-red, and finally light yellow. If strong KOH solution be added to this latter yellow solution, the color is changed to orange-red.[3]

3. *Ferric Chloride Reaction.*—If a few drops of ferric chloride solution be added to an aqueous solution of pure colchicine, no color is produced, but on heating a brownish-red color is developed, which changes to brownish-black. Colchiceine does not give this reaction (the color appearing greenish) although oxydicolchicine and colchicine do.

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[1] Ann. d'Hyg., 1886, **15**, 230.

[2] For other cases in which confusion with ptomaines has occurred see Liebermann, Ber. d. d. chem. Gesellsch., 1876, **9**, 151; and Baumert, Arch. der Pharm., 1887, **225**, 911; Lehrbuch der gerichtl. Chem., 1907, **1**, 406.

[3] See Ekkert, Pharm. Zentralhalle, 1928, **69**, 662.

4. *Zeisel's Reaction.*—If a few drops of ferric chloride be added to the intensely yellow concentrated hydrochloric acid solution of colchicine[1], and the mixture be heated until half the liquid is evaporated, a deep olive-green color appears, which becomes darker on cooling. On shaking this greenish solution with chloroform, this reagent settles out with a garnet-red or brown color, if at least 2 mg. of colchicine be present, while, if there be less of the alkaloid, the chloroform assumes a yellowish tint.

5. *Barillot's Test.*—A small amount of the suspected residue is intimately mixed with 1 cc. of concentrated sulphuric acid and 0.25 gram of oxalic acid. This golden-yellow mixture is sealed up in a small glass tube and heated to 120°C. for one hour, when the tube is opened and its dark reddish-brown contents diluted with water. An excess of alcoholic sodium hydroxide is now added, followed by an excess of acetic acid, when a yellow precipitate is formed. Extract this mixture with chloroform, draw off this solvent and evaporate it to dryness, when a yellow residue is obtained, which becomes violet-red on treatment with concentrated nitric acid and raspberry red with concentrated sulphuric acid. This reaction is especially valuable in differentiating colchicine from morphine and codeine, both of which yield blue colorations, and from ptomaines, which give no similar results.

Biologic Tests.—The frog shows great tolerance to colchicine, requiring from 100 mg. to 1 gram to prove fatal. According to Fühner[2], the frog may be rendered much more sensitive to colchicine by placing the animal in an incubator for a few days before injecting. Such animals are killed in 2 to 5 days by doses of $\frac{1}{10}$ to 1 mg. This peculiarity of the reaction of colchicine with frogs at room and incubator temperature serves to distinguish this alkaloid from others, as no other known poison shows increased effect when given to a warmed frog. The slow onset and progress of the toxic action is, also, characteristic of colchicine.

If frogs be not obtainable, white mice may be used for testing. These animals are killed by a dose of $\frac{1}{20}$ to $\frac{1}{5}$ mg. of colchicine, the symptoms appearing in about 24 hours and progressing slowly.

EMETINE AND IPECACUANHA

Ipecac is the dried rhizome and roots of *Cephaëlis Ipecacuanha*, known in commerce as Rio or Brazilian Ipecac, or of *Cephaëlis acuminata*, known as Cartagena or Panama Ipecac, and yields not less than 1.75 per cent of the ether-soluble alkaloids. Besides the root, the following preparations of ipecac are official: the fluidextract, of which 100 cc. yield not less than 1.35 and not more than 1.65 grams of the ether-soluble alkaloids of ipecac; the syrup, containing 70 cc. of the fluidextract in 1000 cc.; *Pulvis ipecacuanhae et opii* (compound powder of ipecac,

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[1] Fühner (Arch. f. exp. Path. und. Pharm., 1910, **63**, 357) recommends the use of 20 per cent. HCl instead of the concentrated form.

[2] *Nachweis und Bestimmung von Giften auf biologischem Wege*, Berlin, 1911, pp. 76 & 149.

Dover's powder), containing 10 per cent of powdered ipecac and opium; and hydrochloride of emetine.

The active principle of ipecac was for some time supposed to be a single alkaloid, emetine, but the work of Paul and Cowley[1] has shown that there are at least 3 alkaloids present, emetine, cephaeline, and psychotrine, while Hesse[2] believes that there are, in addition two others, namely, hydroipecamine, isomeric with cephaeline, and ipecamine, isomeric with psychotrine. Emetine and cephaeline are the most active of these alkaloids, and are present in largest quantity, the former predominating in Rio ipecac, while the latter preponderates in the Cartagena drug.

Very few fatal cases of poisoning with emetine or ipecac are reported in the literature. Levy and Rowntree[3] have collected 18 cases of poisoning with emetine, none of which were fatal, although they personally report, in addition, one fatal and one non-fatal case. To these should be added the case of Lagane[4] and the two fatal cases reported by Johnson and Murphy.[5] Only 1 case[6] of fatal poisoning with a galenical preparation of ipecac (*vinum ipecacuanhae*) was found in the literature.

Properties.—The constitution of the ipecac alkaloids has been somewhat changed by the work of Carr and Pyman[7] and, also, of Karrer.[8] While Paul and Cowley[9] give as the formula of emetine, $C_{30}H_{44}N_2O_4$, this was changed by Hesse to $C_{30}H_{40}N_2O_4$, and later it was assigned the formula, $C_{29}H_{40}N_2O_4$, by Carr and Pyman, and confirmed by Karrer. Cephaeline differs from emetine in having one less methylene (CH_2) group, and is assigned the formula, $C_{28}H_{38}N_2O_4$; while to psychotrine is given the formula, $C_{28}H_{36}N_2O_4$.

Emetine.—This alkaloid is a nearly colorless, amorphous base, which may become darker in color on exposure to the light. It appears to be uncrystallizable, at least it has not yet been crystallized. It melts at about 68°C. It is only very slightly soluble in water, but dissolves readily in alcohol, ether, acetone, chloroform, and benzene, though only very sparingly in petroleum ether even when hot. On evaporation of any of these solutions, emetine is left as a transparent, varnish-like residue, which is strongly alkaline to litmus and neutralizes acids completely. An alcoholic solution of emetine is levorotatory.

Emetine Hydrochloride ($C_{29}H_{40}N_2O_4 2HCl$)[10].—This salt occurs as a white or very slightly yellowish, odorless, crystalline powder. It is freely soluble in water and in alcohol, its aqueous solution being slightly acid to litmus. Its watery solutions yield precipitates with Wagner's and with Mayer's reagents, as well as with platinic chloride solution. A 5 per cent solution of this salt, mixed with potassium bromide or iodide, yields a dense precipitate, which dissolves on the addition of alcohol, this solution giving, when slowly evaporated, tufts of silky needles of the hydrobromide or hydriodide.

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[1] Pharm. Jour., 1893, 3S., **24**, 61; Ibid., 1894, 3S., **25**, 111, 373, and 690.

[2] Ann. der Chemie, 1914, **405**, 1.

[3] Arch. Int. Med., 1916, **17**, 420.

[4] Cited by Dalimier, Presse méd., 1917, **25**, 33.

[5] Mil. Surg., 1917, **40**, 58.

[6] Harrison, Lancet, 1908, **2**, 536.

[7] Jour. Chem. Soc., 1914, **105**, 1591.

[8] Ber. d. d. chem. Gesellsch., 1916, **49**, 2057.

[9] *Loc. cit.*

[10] The formula given by the U. S. Pharmacopoeia (10th revision) is the old one of Paul and Cowley, namely, $C_{30}H_{44}N_2O_4 2HCl$.

Cephaeline.—When precipitated from a solution of one of its salts by ammonia, it is colorless, but rapidly becomes yellow on exposure to light; it melts at 102°C. By evaporation of a solution in alcohol or ether, the base is left as a faintly yellow, transparent, varnish-like residue, but in a closed vessel a concentrated ethereal solution gradually deposits bunches of delicate silky needles, which melt at 88°C, and, after drying, melt at 119 to 120°C. When freshly precipitated, this crystalline material dissolves in ether, alcohol, acetone, chloroform, methyl alcohol, and hot benzene, although cephaeline is much less soluble in ether, but more readily soluble in petroleum ether, than is emetine. Further, cephaeline differs from emetine in being readily soluble in alkali hydroxides.

Psychotrine.—This alkaloid crystallizes in yellow prisms, which melt at 138°C. It is readily soluble in alcohol, acetone, chloroform, and alkalies, but only sparingly in ether. Its ammoniacal solution shows a blue fluorescence.

Symptoms.—Much depends on the size of the dose, the susceptibility of the individual, and the toxicity of the special commercial preparations used as to the effects of emetine or ipecac. Niccolini[1] has shown that ipecac produces contractions of the intestines, while pure emetine has the opposite effects, although as the ipecac solutions become older their action approaches that of emetine. Whether given by mouth, subcutaneously, or intravenously, toxic doses show much the same symptomatology, the effects being manifested in a relatively short time. There is a copious flow of saliva, followed later by nausea and vomiting, and considerable abdominal pain; frequent and, ultimately, bloody stools; extreme muscular weakness[2]; vertigo; lethargy; convulsive movements of the muscles; peripheral polyneuritis[3]; occasionally, anuria or hematuria; expiratory dyspnea; fall in blood pressure; gradually increasing cardiac weakness, characterized by irregularity accompanied by ventricular fibrillation, and final arrest of the heart in diastole.[4] As ordinarily administered in the treatment of intestinal or oral endamebiasis, the dosage of 0.02 gram of emetine hydrochloride three times daily does not cause such symptoms as the above in all cases. It is wise, however, not to continue such treatment longer than 10 days, following this with a period without medication of about 10 days before a second course is given. Lyon[1] has found that the oral administration of the above amount is almost always followed by the gastro-intestinal symptoms and urges, therefore, the constant subcutaneous administration of the drug. In a certain number of cases, the continuation of this treatment for several days results in an increase in the number of stools with increasing weakness and, often a delirious toxic condition, leading rarely to death. Such actions point to a cumulative toxic effect of non-toxic doses.[2]

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[1] Arch. intern. pharmacodyn., 1922, **26**, 375.

[2] In one of the cases reported by Alvarez (Rev. Med. del Rosario, 1923, **13**, 276) paralysis of the pharynx and difficulty in holding up the head were associated with the extreme asthenia.

[3] See Ardin-Delteil, Azoulay, and Salles, Bull. de la Soc. Méd. des Hôp. de Paris, 1923, **47**, 633; Louis and Trabaud, Ibid., 1273; and de Almeida, Rio de Janeiro Letter, Jour. Amer. Med. Assoc., 1929, **92**, 404.

[4] See Chopra, Ghosh, and De, Indian Med. Gaz., 1924, **59**, 338.

Fatal Dose.—There is considerable divergence of opinion, based upon experimental evidence, as to the lethal dose for animals. Applying to man the figures obtained on animals, Dalimier[3] computes the toxic dose for a man weighing 60 kilos. as 0.12 gram intravenously and 1.8 grams by subcutaneous injection. These figures are closely in accord with those reported by Spehl and Colard[4] of recovery from 1.44 grams, of death from 23½ grains (given in divided doses)[5], of death from a total of 25 grains of emetine hydrochloride in divided doses with periods of intermission[6], and of death from 29 grains in divided doses for 20 days.[7] Dalimier believes that a total dose of 1 gram of emetine hydrochloride is about the limit of safety, while Baermann and Heinemann[8] regard 250 mg. per kilo, as the maximal intravenous dose, a dosage which would, unquestionably, result in quick fatality. In all cases it is important to remember the possibility of cumulative effects and stop the drug at the first sign of untoward results.

Fatal Period.—Owing to the scarcity of reports of death from ipecac or emetine, no definite statements can be made as to the usual fatal period. All that one can say is that death has occurred in 1½ hours from toxic dose of the wine of ipecac. The reports of fatal cases of emetine poisoning indicate that these are of the chronic or cumulative type, so that death is a matter of days rather than of hours.

Treatment.—At the first sign of untoward effects the drug should be discontinued. Tannic acid solutions should be given by mouth and rectum, in order to precipitate the alkaloid present, as well as that reexcreted into the bowel. The patient should be supported by cardiac stimulants, and elimination should be encouraged by diuretics. Later effects are treated symptomatically.

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[1] Amer. Jour. Med. Sci., 1915, **150**, 97.

[2] See Lichtenstein, Geneesk, Tijdschr. Nederl. Indie, 1922, **62**, 490; Abstract in Chem. Abs., 1923, **17**, 420.

[3] Presse méd., 1917, **25**, 33.

[4] Province méd., 1914, **27**, 176.

[5] Johnson and Murphy, Mil. Surg., 1917, **40**, 58.

[6] Johnson and Murphy, *Loc. cit.*

[7] Levy and Rowntree, Arch. Int. Med., 1916, **17**, 420.

[8] Münch. med. Wchnschr., 1913, **60**, 1132 and 1210.

Postmortem Appearances.—The mucous membrane of the stomach and intestines may show marked congestion, although neither of the fatal cases reported by Johnson and Murphy showed any abnormality in the gastro-intestinal tract. In Levy and Rowntree's case, the large intestine showed "no erosions or ulcerations; the mucous membrane of the rectum was slightly flushed and, microscopically, showed marked infiltration with round cells." The heart is stopped in diastole. The other organs show no abnormality, although a terminal pneumonia may appear and give the usual evidence of this disease.

Detection.—Emetine is excreted in small amounts in the urine, but the chief channel of elimination appears to be the intestines and stomach. From the blood emetine rapidly disappears and is stored up in the various organs. Complete elimination of emetine from the system is a matter of months.

As the alkaloids of ipecac are strong, diacid bases, they are not extracted from acid solutions, but only from alkaline. If the solution be alkalinized with sodium hydroxide, emetine may be extracted with ether, but cephaeline remains in the alkaline solution. If, after emetine is removed, the alkaline solution is acidified with hydrochloric acid and then again alkalinized with ammonia, cephaeline is then removed by shaking out with ether. The method of isolating the alkaloids is the general one previously outlined. To obtain the different alkaloids, in pure condition, from the tissues, requires very careful work, so that the residues submitted to examination often show mixtures of the ipecac alkaloids in varying proportion.

1. *Calcium Hypochlorite Reactions.*—If a drop of solution of bleaching powder be applied to a fragment of the residue obtained in the extraction processes and a drop of acetic acid added, a persistent bright orange or lemon-yellow color is produced.

2. *Reactions with Fröhde's Reagent.*—The combined alkaloids of ipecac give on treatment with Fröhde's reagent a yellowish-pink coloration which changes to green or violet, and, on addition of hydrochloric acid, assumes an intense blue coloration. While the violet color obtained before addition of HCl resembles somewhat the color formed on treatment of opium alkaloids with Fröhde's reagent, there should be no confusion between these groups of alkaloids, as the addition of HCl destroys the color with the opium alkaloids.

If one has carefully purified his residues, or if he is testing the pure alkaloids of ipecac, the reactions of each of these are slightly different. The alkaloid emetine gives with Fröhde's reagent a dirty-green color, which turns grass green on addition of HCl. If the reaction be tried upon the hydrochloride directly, the grass-green color is obtained without the addition of the HCl. With pure cephaeline Fröhde's reagent gives no color, but a purple color is shown by impure specimens. On addition of HCl to this purple solution an intense blue color is obtained. Psychotrine gives with Fröhde's reagent a dull-purple color, which is turned into a dull-green on addition of HCl.[1]

3. *Reduction Test.*—If a few drops of a mixture of potassium ferricyanide and ferric chloride be added to a hydrochloric acid solution of the ipecac alkaloids, a beautiful blue (Prussian-blue) color is produced. While this test is of value in showing the possible presence of the ipecac alkaloids, it is not to be regarded as characteristic, as the same reduction test is given by the mixed opium alkaloids. To avoid this possible confusion, treat a portion of the suspected residue with Marquis' reagent[2], which dissolves emetine with a green color that turns yellow, cephaeline yielding a deep yellow color at once, while the opium bases give an intense purple-red color, changing to violet, and finally to blue.

Ergot and Its Alkaloids

Ergot is the dried sclerotium (compact mycelium) of the parasitic fungus, *Claviceps purpurea*, developing on rye plants and replacing the grain of rye (*Secale cereale*), and may, also, be found on other grains and some native grasses. Besides ergot, the only official preparation is the fluidextract, whose strength is such that, when administered by intramuscluar injection to single-comb, white Leghorn cocks in doses not exceeding 0.5 cc. per kilo, it produces a darkening of the comb, corresponding in intensity to that caused by the same dosage of the standard fluidextract of ergot. Numerous propriety preparations of the supposed active principles are sold on the market.

The chemistry of ergot is rather complex and has been the subject of much investigation, which has not, until recently, accomplished a great deal. Fresh ergot is believed to contain at least one or both of the pairs of alkaloids which are specific to ergot: (1) ergotinine and ergotoxine, elaborated by Barger[3] and his associates; and (2) ergotamine and ergotaminine, worked out by Spiro[4] and his colleagues. Besides these alkaloidal bodies, there are present, also, a series of active amines, especially tyramine (p-hydroxy-phenyl-ethylamine), phenyl-ethylamine, iso-amylamine, and histamine (β-imine-azolyl-ethylamine). Tanret[5] adds a further base called ergothioneine, which Barger and Ewins[6] show is

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[1] See Allen and Scott-Smith, Pharm. Jour., 1902, 4S, **15**, 552.

[2] Concentrated sulphuric acid containing a drop or two of 40 per cent. formaldehyde to each 3 cc. of the acid.

[3] See "Alkaloidal Poisons" by Prescott and Webster in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 502, for a complete bibliography.

[4] Spiro and Stoll, Schweiz. med. Wchnschr., 1921, **51**, 525; Spiro, Ibid., 737; Spiro and Dale, Arch. f. exp. Path. u. Pharm., 1922, **95**, 337.

[5] Compt. rend. Acad. des Sci., 1909, **149**, 222.

[6] Jour. Chem. Soc., 1911, **99**, 2336. See, also, Hunter and Eagles, Jour. Biol. Chem., 1925, **65**, 623; Benedict, Newton and Behre, Ibid., 1926, **67**, 267; Hunter and Eagles, Ibid., 1927, **72**, 123; Newton, Benedict, and Dakin, Ibid., 367; Hunter, Biochem. Jour., 1928, **22**, 4; Eagles, Jour. Amer. Chem. Soc., 1928, **50**, 1386; Eagles and Vars, Jour. Biol. Chem. 1928, **80**, 615.

-2-thiolglyoxaline-4 (or 5) -propiobetaine, a base closely related to histidine. Engeland and Kutscher[1] have isolated a further amine, which they call agmatine, a guanidyl-butylamine related to arginine. As these amines are, in reality, putrefactive bases, it is probable that they are derived from the amino-acids by the splitting off of carbon dioxide. Trimethylamine is found as a decomposition product of choline. Besides the above products, we find acetylcholine and a number of physiologically inert substances, so far found only in ergot, such as secale aminosulphonic acid; secalonic acid, a crystalline coloring-matter; sclererythrin, the characteristic red coloring-matter; clavicepsin, a glucoside; ergosterol and fungisterol.

Acute poisoning by ergot may arise either from the eating of bread made from diseased rye or from preparations of the fungus taken internally. Few fatal cases are found in the literature, although many cases of acute poisoning occur.[2] Chronic poisoning with ergot is nearly always due to the eating of bread made from infected rye, widespread epidemics of ergotism occurring during the Middle Ages. Occasionally, however, the medicinal use of preparations of ergot has led to chronic poisoning. Robertson and Ashby[3], in their studies of ergot poisoning among rye bread consumers, report that the average Jewish person consumes about 22.85 grains of ergot daily, which is slightly more than the average daily dose of ergot, and find in these subjects that the symptoms correspond closely with those produced by chronic ergot poisoning.

Properties.—It seems to be believed, at the present time, that the activity of ergot is due chiefly to the alkaloids present, although histamine and tyramine do, certainly, have at least a transitory action.

Ergotinine ($C_{35}H_{39}N_5O_5$) was first isolated in pure condition by Tanret[4], although its properties and chemical formula were elaborated by Kraft[5] and, independently, by Barger and Carr.[6] It is the anhydride of ergotoxine, the two alkaloids being interconvertible, ergotinine being converted into ergotoxine by the action of alkalies and acids in aqueous solution, and ergotoxine being changed into ergotinine by heating the former with methyl alcohol or with acetic anhydride. Ergotinine crystallizes from alcohol in long needles, the sides of which are not quite parallel, but the ends are symmetrically replaced by a pair of faces, and the extinction is straight.[7] If heated rapidly, it melts at 230° to 231°C. At 18°C. it dissolves in 292 parts of ethyl alcohol, in 1020 parts of absolute ether, in 91 parts of ethyl acetate, and in 26 parts of acetone. It is soluble in 77 parts of boiling benzene, in 52 parts of boiling ethyl alcohol, and in 56 parts of boiling methyl alcohol. Extremely soluble in chloroform, but almost insoluble in water, ether, and petroleum ether. Its solutions have a bluish-violet fluorescence, especially when acidified. It is strongly dextrorotatory. The basic properties of ergotinine are feeble, no crystalline salts being known. Ergotinine seems to be almost inert pharmacologically and physiologically.

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[1] Zentralbl. f. Physiol., 1910, **24**, 479.

[2] See Rosenbloom and Schildecker (Jour. Amer. Med. Assoc., 1914, **63**, 1203) for a report of chemical examinations in a case of acute ergot poisoning. Lutier, Presse méd. 1928, **36**, 1436, reports an acute case of ergotinin poisoning.

[3] Brit. Med. Jour., 1928, **1**, 302. See, also, Dilling and Kelly, Ibid., 540.

[4] Compt. rend. Acad. des Sci., 1875, **81**, 896.

[5] Arch. der Pharm., 1906, **244**, 366.

[6] Biochem. Jour., Liverpool, 1907, **2**, 240.

[7] Recrystallization from alcohol should be carried out rapidly, in order to minimize loss of material through transformation of the ergotinine to the ethyl ester of ergotoxine.

Ergotoxine ($C_{35}H_{41}N_5O_6$) was first isolated by Kraft, who called it hydroergotinine, and was later studied by Barger and Carr. It is a white amorphous powder, melting at 160° to 164°C. It is more readily soluble in organic solvents than is ergotinine, especially in cold alcohol, although it is not readily soluble in ether. Its solutions are fluorescent. The salts of ergotoxine crystallize well, the phosphate being more easily purified than the other salts, crystallizing from boiling 90 per cent. alcohol with 1 H_2O and forming slender needles generally arranged in groups radiating from a center. If not pure, the crystals may be spheroid. The phosphate melts at 186° to 187°C., with decomposition, and dissolves in 313 parts of cold and in 14 parts of boiling 90 per cent. alcohol. Both ergotinine and ergotoxine give precipitates with the usual alkaloidal reagents, Mayer's reagent being the most delicate, producing a faint opalescence in dilutions of 1 part per million of these alkaloids. Ergotoxine produces, on intravenous injection in mammals, a somewhat prolonged rise of blood-pressure and, also, contraction of the uterus. It causes the characteristic reaction of ergot on the cock's comb, and is, possibly, responsible for the chronic effects known as "ergotism".

Ergotamine ($C_{33}H_{35}N_5O_5$) is a crystalline alkaloid, insoluble in water, easily soluble in methyl and ethyl alcohol, acetone, and chloroform, and less so in ether. It forms water-soluble salts, one of these, ergotamine tartrate, finding inclusion in New and Nonofficial Remedies under the name of gynergen. In chloroform solution ergotamine is levorotatory. It causes contraction of the uterus, increases the blood-pressure, paralyzes the motor and, possibly, the inhibitory endings of the sympathetic division of the autonomic nervous system, and, in sufficient dosage, causes darkening of the cock's comb. Ergotamine is unstable, on account of its sensitivity to heat, light, and air, and is easily changed by chemical means into ergotaminine.

Ergotaminine.—This is a crystalline isomer of ergotamine. It is much less soluble in ethyl alcohol and other organic solvents, than are ergotamine and ergotoxine. It is strongly dextrorotatory, and is, physiologically, less active than is ergotamine.

Symptoms.—In *acute poisoning* with ergot, the symptoms, which may not appear for some hours, usually begin with vomiting, burning pains in the abdomen, tingling of the extremities, great thirst, weakness, and diarrhea. Swelling of the face and extremities may be observed. The pulse is slow and weak. Abnormal sensations develop in the skin, especially in that of the hands and feet; there are feelings of chilliness, and, later, twitchings or tonic contractions of the muscles. Ataxia, epileptiform convulsions, and mania have been observed. These symptoms are followed by a fall in temperature, and, in many cases, gangrene of the skin is noted. Suppression of the urine, great prostration, coma and death from respiratory and cardiac failure may follow, the fatal issue occurring in a few hours or being delayed for a few days. If the patient be pregnant, and especially if there be a predisposition to miscarriage, abortion followed by severe hemorrhage may occur, leading to death of both mother and child. Powerful contractions of the uterus may be set up by ergot, if there are fibroids present. Smith, McClosky and Hendrick[1] have shown that vitamine B deficient animals have an increased susceptibility to ergotoxine, while rats on a vitamine A deficient diet have a lowered resistance to ergotoxine

Of the *chronic form of ergot poisoning*, known as ergotism, there are two distinct forms, the spasmodic and the gangrenous types. In some epidemics both forms are present, but, as a rule, one form is much more prevalent than the other. The early symptoms are the same in each, and consist in indefinite pains, disturbance of digestion, etc. In spasmodic ergotism there is anesthesia of the fingers and toes, then of the extremities; later, there are tetanic spasms of the muscles, followed, if the patient recovers from the first effects, by contractures of the limbs. Mental weakness or dementia is a not uncommon result. In the gangrenous form of ergotism there is acute pain in one or more limbs; the limb swells, is dark in color, and is very cold. Dry gangrene sets in, and fingers, toes, and even arms and legs and nose fall off, little pain or hemorrhage being noted. Gangrene of internal organs may occur. Cataracts are common. Ergotoxine seems to be largely responsible for these effects.

Fatal Dose and Period.—Ergot and the preparations of ergot vary so greatly in strength that it is impossible to state the fatal dose. The alcoholic fluidextract contains both the alkaloids and the amines, while the aqueous preparations contain chiefly the amines. Thirty grains (1.95 gm.) have caused severe poisoning, but recovery has followed 150 grains (9.72 mg.), while gangrene and death are said to have followed 12 grains (0.77 mg.). One fluiddram of the fluidextract has caused severe poisoning, yet ounce doses have often been given without causing any toxic symptoms. Death has occurred within 1 to 3 days after the appearance of the first symptoms, but death is more likely to follow long-continued use of small or medicinal doses than after one large dose. According to Barger[2], 0.3 gram of ergotoxine per day must be something like the upper limit of the amount required to produce serious gangrene, although idiosyncrasy and malnutrition may cause smaller amounts to be toxic.

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[1] Reprint 1077, Pub. Health. Rep., April 23, 1926.

[2] Pharm. Jour., 1920, **105**, 470.

Treatment.—This consists in washing out the stomach and emptying the bowels by enemata or purgatives, such as calomel or castor oil. In collapse, warm baths with cold affusions are recommended; also, stimulants, such as strychnine, coffee, tea, etc. If gangrene sets in, the parts should be bathed with warm water and wrapped in cotton.

Postmortem Appearances.—There is rapid putrefaction of the tissues. Hyperemia and ecchymotic areas may appear in the stomach and intestines, these tissues not infrequently showing evidence of very intense inflammatory processes. The kidneys, uterus, and lungs may, also, show hyperemia. Microscopic examination sometimes reveals evidence of polyneuritis and endarteritis.

Detection.—On account of the relatively easy transformation of ergotinine into ergotoxine, and vice versa, and, also, because ergotamine is difficultly separable from the former alkaloids, we are compelled to rely upon certain color reactions in identification of residues from cases of ergot poisoning, without reference to the specific alkaloid involved.

1. *Tanret's Test.*—If concentrated sulphuric acid be overlaid with a solution of the alkaloidal residue in ether or ethyl acetate, a transitory orange coloration is produced, which passes through violet to blue.

2. *Rosenthaler's Test.*—If a small amount of the alkaloidal residue be dissolved in a few drops of concentrated sulphuric acid and a trace of ferric chloride solution be added, the mixture acquires an orange-red color changing to deep red, and, at the margins, appearing bluish or greenish-blue.

3. *Keller's Test.*—To a small amount of the alkaloidal residue dissolved in a little glacial acetic acid, add a trace of ferric chloride solution (or of hydrogen peroxide, as recommended by Wolter). Cautiously float this solution on concentrated sulphuric acid, when a brilliant violet or an intense blue is produced at the zone of contact.

Morphine and Opium

Opium is the "air-dried, milky exudation obtained by incising the unripe capsules of *Papaver somniferum* Linné or its variety *album* De Candolle (Fam. *Papaveraceae*)." In its normal, moist condition opium yields not less than 9.5 per cent. of anhydrous morphine. This poppy is grown chiefly in India, China, Egypt, Persia, and Asia Minor, but has been cultivated in colder climates. Opium is a highly complex body, over 20 alkaloids having been isolated therefrom with others probably undiscovered. The most important of these are morphine, codeine, papaverine, narcotine, and thebaine, while the less important ones (so far known) are pseudomorphine, codamine, laudanine, laudanosine, meconidine, lanthopine, crytopine, protopine, papaveramine, rhoeadine, oxynarcotine, narceine, hydrocotarnine, gnoscopine (racemic narcotine), and tritopine. These alkaloids exist in combination, especially with sulphuric and meconic acids, while a few are united with acetic and lactic acids. "With one or two exceptions, the alkaloids of opium are strictly peculiar to *Papaver somniferum;* while, on the other hand, the poisonous alkaloid sanguinarine, which is present in all other papaveraceous plants, does not appear to exist in Papaver." Morphine, codeine, and thebaine are derivatives of pyridine and phenanthrene, while narcotine, papaverine, and most of the other alkaloids are derivatives of benzene and isoquinoline. "In morphine the narcotic action is the most striking feature, but as the successive members are taken up, this effect becomes less marked than the reflex stimulation, until in thebaine practically no depression can be made out, and the symptoms resemble those of strychnine exactly. In man morphine is much the most dangerous of the opium alkaloids, because death is produced in the narcotic stage through asphyxia. In most animals, however, thebaine, codeine and laudanine are more toxic, because the failure of respiration does not occur in the stage of depression, but during the convulsions."[1] It is thought by some that opium is a better narcotic than morphine, although most observers seem to agree that the cerebral action of these drugs is practically identical. On this basis, however, there has been introduced *pantopon*, a preparation of all the alkaloids of opium in the proportion in which they exist in Smyrna opium. As the alleged superiority of opium over morphine as a narcotic is supposed to be due to the presence of narcotine in the former, *narcophine* (morphine-narcotine meconate) has been advocated as superior to morphine in narcotic power, while less depressant to the respiration.

Statistics of Poisoning.—It is quite impossible to give any exact figures as to the number of cases of poisoning by opium and its alkaloids, as many of these cases do not find their way into the tables of statistics. By far the most of the cases are either accidental or suicidal. According to Witthaus[2], "from thirty-five to forty per cent. of all accidental and suicidal poisonings are by opiates", a figure which would seem to be much too high, if we are to include the accidental and suicidal deaths from illuminating gases in the list. That many such cases do, however, occur is shown by the figures of the Medical Examiner's Office in New York City. Thus, in 1918 there were reported 40 accidental deaths from morphine and 14 from opium, and 2 suicidal cases; in 1919, 34 accidental cases from morphine and 6 from opium, and 1 suicidal; in 1920, 33 accidental cases from morphine and 4 from opium, with 1 suicidal from morphine; in 1926, 32 accidental deaths from morphine and 17 from opium, with 5 suicidal cases from morphine; and in 1927, 24 accidental cases from morphine and 17 from opium, with 3 suicidal cases from morphine. Witthaus was able to find in the literature (up to 1911) only 11 homicidal cases from opium, and 12 from morphine. Opium and its alkaloids must, therefore, be regarded as causing a large number of deaths.[3]

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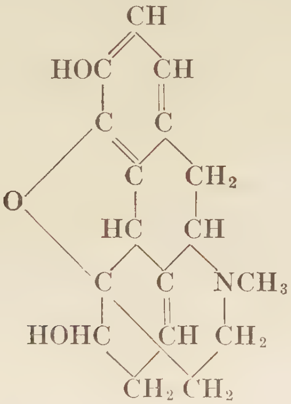
[1] See *Pharmacology and Therapeutics* by Cushny, 9th ed., revised by Edmunds and Gunn, 1928, p. 270.

[2] *Toxicology*, 1911, p. 948.

[3] For a bibliography of the recent cases see "Alkaloidal Poisons" by Prescott and Webster in *Legal Medicine and Toxicology* by Peterson, Haines & Webster, 1923, **2**, 527.

Properties.—The official preparations of opium, under the 10th, revision of the United States Pharmacopoeia are opium, opium granulatum, opium pulveratum, tinctura opii, tinctura opii camphorata, and pulvis ipecacuanhae et opii, the defining descriptions of which may be obtained from the Pharmacopoeia.

Morphine ($C_{17}H_{19}NO_3$).—Morphine is a monacid, tertiary base, whose nitrogen is combined with 3 atoms of carbon. The 3 oxygen atoms have different characteristics, one being a phenolic hydroxyl, one alcoholic, and the third indifferent, forming a so-called bridge-oxygen. Of the 17 carbon atoms, 14 belong in the phenanthrene nucleus, which forms the base of the morphine molecule. While, possibly, not absolutely settled, the graphic structure is represented as follows:



The free base morphine is no longer official. It occurs in colorless or white, shining, rhombic prisms, in fine needles, or as a crystalline powder, odorless, and permanent in the air. One gram of morphine dissolves in 3340 cc. of water, 210 cc. of alcohol, 1220 cc. of chloroform, 6250 cc. of ether, and in 100 cc. of lime water at 25°C.; also in 1075 cc. of boiling water and 98 cc. of boiling alcohol; in 125 cc. of amyl alcohol at ordinary temperature and in 50 cc. of hot amyl alcohol; insoluble in benzene. The organic solvents dissolve morphine in the form of an amorphous powder or in the freshly precipitated condition much more readily than when it exists as a crystalline precipitate. Morphine is precipitated from its solutions by the addition of alkali hydroxides, carbonates, or bicarbonates, but the precipitate with the hydroxides dissolves readily in excess of the reagent, so that neither sodium or potassium hydroxide should be used to alkalinize mixtures suspected of containing morphine, as the immiscible solvent will not extract the alkaloid from such solutions.

Morphine Hydrochloride ($C_{17}H_{19}NO_3HCl.3H_2O$).—This occurs as white, silky, glistening needles or cubical masses, as a white crystalline powder, odorless, and permanent in the air. One gram of the hydrochloride dissolves in 17.5 cc. of water and in 52 cc. of alcohol at 25°C.;

also in 0.5 cc. of boiling water and in 46 cc. of alcohol at 60°C. It is soluble in glycerin, but insoluble in chloroform and in ether. Its aqueous solution is neutral or slightly acid to litmus.

Morphine Sulphate ($(C_{17}H_{19}NO_3)_2H_2SO_4.5H_2O$).—This occurs in white, feathery, silky crystals, or cubical masses, or as a white crystalline powder, odorless, and stable in the air. One gram is soluble in 15.5 cc. of water and in 565 cc. of alcohol at 25°C., also in 0.7 cc. of water at 80°C. and in 240 cc. of alcohol at 60°C. It is insoluble in chloroform and in ether. Its aqueous solution is neutral or slightly acid to litmus.

Codeine ($C_{18}H_{21}NO_3$).—This alkaloid is present in opium in the proportion of 0.2 to 0.8 per cent., its quantity averaging about 1/24 that of morphine. Chemically, codeine is methyl-morphine, the methyl group replacing the hydrogen of the phenolic group of morphine. The alkaloid itself, and the phosphate and sulphate are official. Codeine crystallizes from dry ether, carbon disulphide, or benzene in anhydrous prisms melting at 155°C. From water or water containing ether it crystallizes with 1 molecule of water of crystallization in colorless, translucent, crystals, or as a white crystalline powder, odorless and slightly efflorescent in warm air. These latter crystals melt at 152° to 153°C., and when rendered anhydrous by drying at 80°C. melt between 154° and 156°C. One gram of codeine dissolves in 120 cc. of water, 2 cc. of alcohol, 0.5 cc. of chloroform, 18 cc. of ether, and in 13 cc. of benzene at 25°C. It is readily soluble in amyl alcohol, but difficultly soluble in petroleum ether. A saturated aqueous solution of codeine is alkaline to litmus paper, and is levorotatory. It dissolves very easily in acids to form salts, from which solutions it is precipitated by sodium or potassium hydroxide, but not by ammonium hydroxide.

Codeine Phosphate ($C_{18}H_{21}NO_3.H_3PO_4.2H_2O$).—This salt occurs in fine, white, needle-shaped crystals, or as a white, crystalline powder, odorless and very efflorescent. One gram of codeine phosphate dissolves in 2.3 cc. of water, 325 cc. of alcohol, 4500 cc. of chloroform, and in 1875 cc. of ether at 25°C.; also in 0.5 cc. of water at 80°C., and in 125 cc. of boiling alcohol. Its aqueous solution is acid to litmus paper.

Codeine Sulphate ($(C_{18}H_{21}NO_3)_2H_2SO_4.5H_2O$).—This salt occurs in long, glistening, white, needle-shaped crystals or rhombic prisms, or as a crystalline powder, odorless and efflorescent. One gram of codeine sulphate dissolves in 30 cc. of water and in 1280 cc. of alcohol at 25°C.; also in 6.5 cc. of water at 80°C. and in 440 cc. of alcohol at 60°C.; insoluble in chloroform and in ether. Its aqueous solution is neutral or not more than faintly acid to litmus or methyl red.

Heroine ($C_{21}H_{23}NO_5$).—Heroine is a synthetic derivative of morphine prepared by the acetylization of morphine, the hydrogen atoms of the alcohol and phenol groups of morphine being replaced by the acetic radical. It is, therefore, diacetylmorphine. Although formerly official, neither the base itself nor its hydrochloride find inclusion in the present Pharmacopoeia. This artificial alkaloid forms white prisms or a white crystalline powder having no perceptible odor, with a bitter taste, and showing an alkaline reaction to litmus. It melts between 171.5° and 173.5°C. One gram of heroine dissolves in about 1700 cc. of water, 31 cc. of alcohol, 1.4 cc. of chloroform, and in 100 cc. of ether at 25°C. Readily soluble in benzene. Heroine is easily hydrolyzed by heating with water or dilute acids, and especially by alkalies, to morphine and acetic acid. This deacetylization takes place to a great extent in the system, but not in the stomach, so that in cases of poisoning it has been the usual thing to find residues showing the reactions for morphine itself, instead of those of heroine. This alkaloid is precipitated by alkalies, but is soluble in excess of these agents, so that alkalinization should be carried out with weak alkalies.

Diacetylmorphine (Heroine) Hydrochloride ($C_{21}H_{23}NO_5HCl.H_2O$) occurs as a white crystalline powder without odor. Its aqueous solution is neutral or only faintly acid to litmus. It melts at about 230°C. with decomposition. One gram of this salt dissolves in 2 cc. of water at 25°C.; soluble in alcohol, but insoluble in chloroform or ether at 25°C.

Ethylmorphine (Dionine) Hydrochloride ($C_{19}H_{23}NO_3HCl.2H_2O$) is an official synthetic alkaloid prepared by ethylation of morphine. It occurs as a white or faintly yellow, microcrystalline powder, having no odor. Its aqueous solution is neutral to litmus paper. One gram dissolves in 8 cc. of water and in 22 cc. of alcohol at 25°C. It is slightly soluble in ether and in chloroform.

Symptoms.—In cases of acute poisoning by opium or by morphine taken by mouth the effects begin to appear, in many cases, in from 20 to 40 minutes. If the drug be taken hypodermically the symptoms appear earlier. Quantities much larger than just enough to be fatal usually cause a preponderance of comatose symptoms, sometimes from the first. On the other hand, a poisonous quantity not more than enough to be fatal gives rise to the more pronounced and prolonged initial stage, that of mental exaltation and increased cardiac action. Still wider deviations of symptoms and the time of their accession result from the individuality of the nervous system.

The train of symptoms is much as follows: A sense of mental exhilaration and physical ease, with both a quickening and a strengthening of the pulse. Then follow dizziness and heaviness of head, nausea, languor, and drowsiness, the pulse being reduced in frequency some time before it is reduced in force. Nausea comes on early in some cases, and if there is vomiting as an effect of the poison, the earlier it occurs the more thorough it is likely to be. In some cases there are itching of the skin and, even, a sudden eruption. As a rule the secretions other than those of the skin are checked. The desire to sleep increases and returns irresistibly in spite of efforts to keep awake. With approaching stupefaction, there is gradual loss of muscular power and a diminished sense of feeling. Meantime, the pupils of the eyes have become contracted, which is a distinctive symptom, although there are cases in which there is no contraction, but these must be regarded as the exception. The sensitiveness of the conjunctiva is diminished, and the pupils fail to respond to light. The respirations have become less and less frequent, and are finally reduced, in some cases, to three or four a minute, with stertorous breathing. Shallow respiration is often observed. A peculiar respiratory pause or interval is found in some cases, lasting ½ minute or longer, followed by somewhat rapid breathing, becoming then gradually slower until, after 20 or 30 respirations, there is another pause, the Cheyne-Stokes respiration. Cases have been observed in which the pupil contracts at the time of the pause and dilates during the rapid breathing, and the stupor has been found to vary with the same alternation. In other cases the respiration is calm, being gradually reduced from first to last. The breathing gives an index of the action of the poison on the respiratory nerve-center, the one point where death is threatened and defense is made. With slow or interrupted respiration the face grows bluish, the lips become livid, the extremities cold, and the body temperature is reduced. The characteristic effect of morphine is a diminution in the rhythm of the center, which remains susceptible to reflex stimulation, but is unable to accelerate the discharge of impulses to the same extent as normally. There are, therefore, two poisons to consider, the morphine and the carbon dioxide, which may be accountable for the asphyxia. The surface of the body is usually moist and clammy, although occasionally the skin may be warm and dry. The stupor becomes deeper, while the pulse, which has been full but growing slower, finally becomes weak. Generally at the last, just before the final asphyxia, the pupils dilate. During the intoxication, there is, according to Sollier,[1] an increase in both the red and white cells, a change in the differential count, and a considerable increase in the viscosity of the blood. Sometimes convulsions occur in the later stages, more often with children, and in some cases the convulsions have been of a tetanoid character.

Codeine resembles morphine in the general features of its action, although it is much less poisonous. It depresses the brain, and causes an exaltation of the activity of the lower parts of the central nervous system. Its depressant action is not so powerful nor as enduring as that of morphine, while the stimulation is more evident and involves not only the cord but, also, the medulla and lower parts of the brain. Small quantities of codeine produce sleep, but this is not so deep and restful as that with morphine. Somewhat larger quantities, instead of inducing sleep, increase the restlessness and cause a considerable exaggeration in the reflex excitability. The respiration is not so much slowed as after morphine, and the excitability of the center is practically unchanged. The pupil is slightly contracted during the codeine sleep, but dilates when the excitement stage follows. According to Lewin, doses of 0.8 gram of codeine produce muscle weakness, disturbance of vision, myosis or mydriasis, vertigo, loss of consciousness, slight delirium, muscular contractions, acceleration of the pulse, dyspnea, and collapse.

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[1] Bull. acad. méd., 1922, **87**, 428.

Heroine resembles morphine in its general effects, but acts more strongly on the respiration and less on the cerebral functions. The respiration is rendered slower with less mental depression, the slowness in the breathing being, apparently, compensated for by its greater depth, so that the actual diminution of the air inspired is not proportional to the decrease in the number of the respiratory movements, although Cushny believed that such is certainly not invariably true. The more common symptoms of poisoning, as revealed by the literature, are headache, disturbance of vision, myosis, slow, small, regular pulse (although it may at times be rapid), restlessness, cramps in the extremities, slight cyanosis, respiration slow and deep, death occurring from respiratory paralysis.

Chronic Poisoning.—It is not within the scope of this work to discuss the question of habituation ("opium habit"), or the chronic use of morphine or heroine, as this is more of a direct medical and economic problem than one of toxicology. Besides the ordinary cases of adults who habitually take the drug by mouth or hypodermically, or who inhale the fumes of crude opium, there are many obscure cases of infants habitually dosed with nostrums containing morphine, and of persons suffering chronic poisoning from the continued application of opiate dressings, while the heroine habitue usually takes his drug in the form of snuff.

The subjects of the opium habit, though known to be able to bear without injury large quantities of the poison—3 or 4 grams or more daily—yet sometimes fall as the victims of acute poisoning by the same drug. The opium eater may exceed his own limit so far as to forfeit his acquired toleration, or this tolerance may give way under some unusual condition of the system.[1] As to the mechanism of habituation and tolerance little of a definite nature is known. It has been alleged that the continuous ingestion of morphine causes the appearance in the blood serum of a substance having a protective immunizing effect against the drug, but Pellini and Greenfield,[2] and later DuMez and Kolb[3], have shown that the blood of human addicts does not contain transferable immunizing substances against the action of morphine. These former workers[4] have shown, also, that there is not, at least in dogs, the production of any specific toxic substance, as Valenti[5] claims.

Absorption and Elimination.—Absorption of opium and its alkaloids occurs from all mucous membranes, although most cases of poisoning arise from absorption through the gastrointestinal tract. That it does occur, however, from the respiratory tract is shown in opium smokers, while absorption from the nasal and buccal cavities is indicated in the case of the girl poisoned while making morphine tablets.[1]

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[1] See *The Opium Problem* by Terry and Pellens, New York, 1928; Light, Arch. Int. Med., 1929, **44**, 870.

[2] Arch. Int. Med., 1920, **26**, 279.

[3] Pub. Health Rep., 1925, **40**, 548.

[4] Pellini and Greenfield, Arch. Int. Med., 1924, **33**, 547.

[5] Arch. f. exp. Path. und Pharm., 1914, **75**, 437.

According to Cushny[2], "When given subcutaneously to rabbits morphine can be largely recovered from the stomach contents, from the walls of both stomach and intestine, from the muscles of the body, and from the urine. In the early hours after the injection of the alkaloid it appears in largest amounts in the stomach contents while smaller amounts are found in the urine. Later the amount in the urine is increased while the gastric excretion is lessened so that almost equal amounts may be found in both stomach and bladder. The bowel probably does not take part in the excretion, such morphine as escapes in the feces being derived from the gastric contents. Most of the morphine therefore is eliminated from the body in the urine. Considerable amounts are found stored in the muscles . . . In acute morphinism very little morphine is destroyed in the body, as even after sixteen hours (in rabbits) over 90 per cent of the drug administered may be regained from the various tissues and excretions. In chronic morphinism destruction of the morphine doubtless takes place and there is in addition a very considerable storage of the drug in the muscles." The work of Hatcher and Davis[3] would seem to indicate that at most traces of morphine are excreted into the stomach of the cat and dog after subcutaneous, intramuscular or intravenous injections of varying amounts. Takayanagi[4] shows that the excretion of morphine in the urine may, under certain circumstances, greatly exceed the amount eliminated through the alimentary tract with the feces. His studies indicate that when a single dose of morphine is given, the urinary excretion is delayed and slow, while in cases in which it has been previously administered, the urinary excretion, resulting from a subsequent dose, may be accelerated. When tolerance has been established, however, the excretion through the kidney is lessened. There is little question that some of the morphine is destroyed in the system in acute morphine poisoning, although Homburger and Munch[5] find that 97.5 per cent. of the morphine injected into cats and rabbits could be recovered if the examinations be started soon after death. In the chronic types of poisoning, however, relatively large amounts are destroyed or converted into oxidation products, such as oxydimorphine (pseudomorphine), such change taking place, possibly in the brain and the liver[6], although Rübsamen[7] was unable to detect any decomposition of morphine by the brain substance of normal animals outside the body.

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[1] Barnes, Phila. Med. Jour., 1901, **8**, 1100.

[2] *Pharmacology and Therapeutics,* 9th ed. revised by Edmunds and Gunn, 1928, p. 267.

[3] Jour. Pharm. and Exp. Therap., 1925, **26**, 49.

[4] Arch. f. exp. Path. und Pharm., 1924, **102**, 176.

[5] Jour. Amer. Chem. Soc., 1916, **38**, 1873.

[6] See Cloetta, Arch. f. exp. Path. und Pharm., 1903, **50**, 453: Scott, Loria and Tardo, Arch. Int. Med., 1925, **35**, 472, Cloetta, in *Lehrbuch der Toxokologie,* by Flury and Zangger, 1928, 280.

[7] Arch. f. exp. Path. und Pharm., 1908, **59**, 227.

Fatal Dose.—It is very difficult to state the usual fatal dose of opium or of morphine, as individuals differ greatly in their resistance to the drug, some having an unusual susceptibility (idiosyncrasy) to its action, while others prove markedly resistant, due, possibly, to their strong and well-nourished constitution and, especially, to a normal circulatory apparatus. Children, especially nurslings, and elderly adults are much more susceptible to the action of opiates, than are older children and adults below 60 years of age.

It may safely be said that 2 grains (0.13 gram) of morphine sulphate is so poisonous a quantity when swallowed as to endanger the life of a person not accustomed to the drug. According to Haines[1], "The average minimum fatal dose of opium for an adult may be placed at about 4 or 5 grains, and that of morphine at about 1 grain", while Hofmann-Haberda[2] states that the lethal dose of opium is 1 to 2 grams and that of morphine and its salts averages 20 to 40 cg. A quantity of morphine just above the limit of a medicinal dose in any case is really on the border of a *poisonous quantity* in that case. Given a barely poisonous quantity—that is the smallest one "tending to produce death"—it will depend on a great number of factors just how much more would be enough to carry out the *tendency* to its fatal conclusion.

Fatal Period.—The duration of fatal acute poisoning by morphine or opium is, in a considerable proportion of cases, from six to twelve hours, although cases are reported of death in 45 minutes[3] and of a duration of 3 days[4]. "Of 41 fatal cases, 32 died in times varying from five to eighteen hours, about one-half in from six to ten hours, the most usual time being about nine or ten hours after the poison had been taken. If a patient survives twenty-four hours, the prognosis is favorable."[5]

No fatal cases of codeine poisoning are found in the literature. Doses of 0.3 gram would, probably, produce very unpleasant, if not dangerous symptoms, although recovery is reported from doses of 0.518 gram (8 grains) in 2 cases. As regards heroine, it is to be said that this alkaloid is, undoubtedly, more toxic than is morphine. Cases of poisoning have been reported from doses of 0.005, 0.01, 0.05 and 0.167 gram, while death has followed a dose of 0.6 gram. In the cases reported by McNally[6], the fatal dose is unknown but 0.3022 and 0.0436 gram of alkaloid were recovered from the tissues.

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[1] Hamilton's System of Legal Medicine, 1894, **1**, 441. See, also, Woodman and Tidy, *Forensic Medicine and Toxicology*, 1877, p. 336.

[2] *Lehrbuch der gerichtlichen Medizin*, 11te Aufl., 1927, p. 898

[3] See Coale, Amer. Jour. Med. Sc., 1850, n. s. **19**, 71; Lyman, Ibid., 1854, n. s. **28**, 384; and Ebertz, Vrtljschr. f. ger. Med., 1873, n. F., **18**, 280.

[4] See Maschka, Prag. med. Wchnschr., 1887, **12**, 437; and Penny, Med. Sentinel, 1893, **1**, 299.

[5] Woodman and Tidy, *Forensic Medicine and Toxicology*, 1877, p. 335.

[6] Jour. Lab. and Clin. Med., 1917, **2**, 570. See, also, Hohberg and Beck, Deutsch. Arch. f. d. ges. ger. Med., 1928, **12**, 112.

Treatment.—The first requisite in cases of acute morphine poisoning is to remove the poison from the stomach to prevent further absorption. This should be done with copious lavage, using finely powdered charcoal as an adsorbent and a $\frac{1}{2}$ to 1 per cent aqueous solution of potassium permanganate to oxidize the morphine. Tannic acid is probably of little value, as it does not form readily an insoluble precipitate. Whether frequent lavage of the stomach is of value, as has been claimed by many on the basis of the excretion of morphine into the stomach, may be questioned in view of the work of Hatcher and Davis[1], although such procedures would, undoubtedly, be of value, if death had occurred in the early stages of poisoning. Emetics have been advised, but their use seems questionable, especially the employment of apomorphine, as this may increase an existing asthenia.

Stimulation of the respiration and of muscular movement is a necessity to overcome the depression of the respiratory center. The patient should be kept awake, if possible, by walking him up and down between assistants, and by flicking his body with a wet cloth and by cold cloths applied to the head and face. Artificial respiration, with inhalation of pure oxygen[2], may be necessary, and should be employed when the respiration becomes greatly embarrassed. Atropine sulphate may be given hypodermically, the earlier the better, in doses of 2 mg., but its action must be watched and stopped when mydriasis occurs.

General stimulants, such as strychnine and caffeine, should be pushed to improve the circulation and respiration. The patient should be kept warm by hot foot-baths, friction, etc. The bowels should be cleared by high enemas, to prevent the possibility of a relapse from reabsorption of morphine.

Postmortem Appearances.—The findings at autopsy are not characteristic. The pupils are, occasionally, contracted, but more often they are of ordinary size or, even, dilated, as they may be before death. The blood vessels of the brain are usually very full, and, frequently, there is found an effusion between the membranes and into the ventricles. Congestion of the lungs is generally present. The blood is, ordinarily, fluid and dark in color. If opium in substance or as the tincture has been taken, the characteristic opium odor will be perceived on opening the stomach. No local irritation of the mucous membrane of the stomach or intestines is noted, but the intestines may be rather markedly contracted, especially if death is rapid.

Detection.—In cases of acute morphine poisoning the stomach and its contents, the intestines and feces, and, especially, the urine[3] should be examined, as these are the chief channels of excretion. Some of the morphine however remains in the organs, the liver and kidneys being, probably, the more important, while the blood, spleen, brain and spinal cord will, also, yield their quota, that present in the liver and kidneys being, according to Marquis, in a changed form, and that in the other parenteral organs being, possibly, in a conjugated state.

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[1] Jour. Pharm. and Exp. Therap., 1925, **26**, 49.

[2] See McCurdy, Jour. Amer. Med. Assoc., 1929, 92, 1927, who employs CO_2—O_2 mixtures.

[3] See Fry, Light, Torrance and Wolff, Arch. Int. Med., 1929. **44**, 862 for excretion in addicts.

Morphine is relatively easily oxidized, the first product of this change being oxydimorphine (pseudomorphine, $(C_{17}H_{18}NO_3)_2$), while further oxidation yields a number of distinctive color-products, undetermined members of known series, variable derivatives of the several color roots of morphine. In spite of this oxidation, morphine resists putrefaction for long periods of time, so that it may be detected in the presence of cadaveric material after many months. Thus, Palet[1] was able to recover this alkaloid from decomposed viscera seven months after death; Ipsen[2] detected morphine after a period of nine months; Doepmann[3] detected unchanged morphine 11 months after it had been added to meat; while Grutterink and van Rijn[4] showed the presence of morphine after it had been in a cadaver for 2½ years.

On the other hand, there are many cases of acute poisoning, in which the examination by competent chemists has been started soon after death, and, yet, no morphine has been found. There is every reason to believe that it is not uncommon in cases of fatal poisoning by morphine for the alkaloid to disappear beyond the reach of analysis—that is, to become so far attenuated that it does not meet the limit of its analytic recovery from the organs in which it is deposited. Just why such conditions may obtain in one case and not in another is impossible to state.

Considerable discussion has arisen in the past as to the presence of certain ptomaines, which have been isolated in some forensic cases, and which gave some reactions simulating those for morphine. In none of the cases, however, have these reactions been identical in every respect, although there has been similarity, but this is not sufficient to warrant conclusions. Exact duplication of the results with the unknown and known substances must obtain. While admitting the possibility of influences of putrefactive bases upon the reactions for morphine, the analyst should take special precautions in the purification of his residues and reagents, and should make his identification tests side by side with specimens of known morphine. It will be found, if this be done, that the reactions with these putrefactive bases vary in color or sequence of color from those given by the pure alkaloid in some one or more of its characteristic tests. For this reason, pseudoreactions must be eliminated and insistence laid upon unequivocal color and chemical reactions.

In extracting morphine from the tissues, the method outlined for alkaloids may be followed, care being taken to heat the finely divided material in a closed flask, fitted with a reflux condenser, at a temperature not above 70°C. The process of fractional precipitation of the protein materials, as advocated by Haines[1], is recommended. The choice of the immiscible solvent to be used to extract the morphine will depend much on the experience of the worker, but the writer prefers the chloroform-alcohol mixture (chloroform containing 10 per cent. by volume of alcohol) as recommended by Kippenberger[2], although amyl alcohol is, probably, a better solvent but is prone to form annoying emulsions. Owing to the relatively slight solubility of morphine in the chloroform-alcohol mixture, this solvent should be used hot and several extractions should be made, until an evaporated portion of the extract shows no further reaction with Marquis' reagent. In alkalinizing the acid solution, before extraction with the immiscible solvent, ammonia or sodium bicarbonate should be used, as the stronger alkali hydroxides readily dissolve the alkaloid first precipitated. Balls and Wolff[3] advise adjusting the solution to a pH of 9, approximately the isoelectric point of morphine. Should the chloroform-alcohol residue appear impure, especially should it show any trace of color, this may be purified, as recommended by Russwurm, as follows: Dissolve the residue in hot amyl alcohol and shake the solution thoroughly with several portions of hot water containing a few drops of dilute sulphuric acid, which will dissolve out the morphine, while the amyl alcohol retains most of the coloring matter. Separate the aqueous solution, alkalinize with ammonia or sodium bicarbonate, and extract several times with hot chloroform-alcohol mixture.[4] Place the combined chloroform-alcohol extracts in a dry flask, add a few crystals of anhydrous sodium sulphate to remove adherent water, and filter through a dry filter into a dry glass-stoppered measuring cylinder. Portions of this solution may be evaporated to dryness for the color-tests to be described, and an aliquot part may be used for quantitative determinations.

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[1] Ann. Soc. quim. Argent., 1919, **7**, 22. Abstract in Chem. Abs., 1919, **13**, 3203.

[2] Vrtljschr. f. ger. Med., 1913, 3 F., **45**, 1 supp., 198.

[3] Chem.-Ztg., 1915, **39**, 69.

[4] Pharm. Weekblad, 1915, **52**, 423.

Chemical Tests.—The tests for morphine are of several different types, some being peculiar to the morphine molecule, some depending upon the presence of the free hydroxyl group in the molecule, others being caused by the reducing action of morphine, and still others being due to the conversion of morphine to apomorphine.

1. *Fröhde's Test.*[5]—This is a changing color test in which morphine is oxidized and molybdic acid reduced. The test is made upon the dry material obtained by evaporation of a few drops of the chloroform-alcohol solution. Place a small amount of this residue in a white porcelain testing dish and treat it, in the cold, with one drop of the freshly pre-

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[1] See page 344.

[2] Ztschr. f. anal. Chem., 1900, **39**, 201 and 290. See, also, Williams, Amer. Jour. Pharm., 1914, **86**, 308; and Tingle, Ibid., 1918, **90**, 689, 788, and 851.

[3] Jour. Biol. Chem., 1928, **80**, 379.

[4] See Gadamer, *Lehrbuch der chemischen Toxikologie*, 2te. Aufl., 1924, p. 545; and Autenrieth, *Detection of Poisons*, 6th Amer. Ed., translated by Warren, 1928, p. 224.

[5] For the preparation of the reagent see page 606. Instead of the molybdic acid prescribed by Fröhde, one may use sodium molybdate, as recommended by Buckingham.

pared reagent. If morphine be present there will be noticed a deep purple color fading to violet, passing through blue into a dirty green, and changing slowly into yellow and, finally, to faint pink. These changes are the more rapid the less the amount of morphine. If the quantity of morphine be large, the violet color may persist for a long time. These colors vanish on the addition of water. With codeine, this test gives a yellowish color, which soon changes to deep green and, finally, blue. With heroine the reaction is much the same as with morphine, the purple gradually changing to blue; while with apomorphine the initial color is a dirty green, which changes gradually to blue. The putrefactive bases do not appear to give blue colors with this reagent.[1] This reaction is quite distinctive with pure morphine, but one should be guarded in his deductions from this test alone, owing to the possible influence of impurities in the residue obtained in forensic cases. The result should, always, be compared with that of a control using known pure morphine. The Fröhde test is sensitive to the presence of 0.01 mg. of morphine.

2. *Marquis' Test.*—The reagent for this test consists of 3 cc. of pure concentrated sulphuric acid to which 2 or 3 drops of 40 per cent. formaldehyde (formalin) have been added. If the dry residue, on white porcelain, is touched from the point of a glass rod with this reagent, an intense purple-red color, changing to violet, and, finally, to pure blue is obtained if morphine be present. This reaction is quite distinctive, although the alkaloids related to morphine show somewhat similar reactions. Thus, codeine does not give the initial purple, but strikes a violet changing to blue; apomorphine gives first a violet, then a blackish-green; oxydimorphine shows a green color, which changes to a flame red; dionine gives a dark blue-violet; while heroine shows the same colorations as does morphine. A marked reaction is given by 0.02 mg. of morphine.[2]

3. *Husemann's Test.*—This test is a modification of an earlier one introduced by Erdmann, and depends upon the conversion of morphine to apomorphine. If a small amount of the solid residue be moistened with a few drops of pure concentrated sulphuric acid and warmed on the water-bath for ½ hour, or heated over a small flame for a few minutes, a slightly reddish color may appear. If, now, we add to this residue 1 or 2 drops of concentrated nitric acid, or a crystal of potassium nitrate, a reddish-violet color appears soon changing to blood red and then fading into yellow. This same test is shown by the alkaloids codeine, oxydimorphine, and apomorphine, and the synthetic products, heroine, dionine, and peronine. Its limit of delicacy is about 1:40,000. If concentrated nitric acid, alone, be added to a morphine residue, an orange red to deep red color, changing to yellow, is observed. Brucine gives this same coloration, which, however, is restored to red or violet on addition of

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[1] See Rosenbloom and Mills, Jour. Biol. Chem., 1913, **16**, 327; and Rosenbloom, Ibid., 1914, **18**, 131.

[2] See Levine and Magiera, Jour. Lab. and Clin. Med., 1927, **12**, 773; Levine and Fulton, Ibid., 1929, **14**, 350.

stannous chloride or of ammonium sulphide, while that given by morphine is not changed by these reagents.

Fulton[1] believes that it is better to heat the morphine and acid to a temperature of 40° to 50°C. rather than to the higher temperature. His procedure is as follows: Dissolve a small amount of the residue in about 1 cc. of pure concentrated sulphuric acid, place the test tube in a beaker of water with a thermometer, and heat to 40° or 50°C. If 5 to 10 drops of this heated solution be placed in a porcelain dish and be treated with a very small trace of concentrated nitric acid or a tiny crystal of potassium nitrate and the mixture stirred, an orange-red color is produced which changes at once to purple and soon to gray blue and then to dull green. If an excess of nitric acid be used the solution becomes and remains red or orange-red.

4. *Pellagri's Test.*—This test, like that of Husemann, depends on the formation of apomorphine. Dissolve a small amount of the residue obtained in the extraction process in 2 or 3 cc. of concentrated hydrochloric acid and add a few drops of concentrated sulphuric acid. Evaporate this mixture in a porcelain dish on the boiling water-bath, until the HCl has disappeared and continue the heating for 1/4 to 1/2 hour longer, when a dirty red or violet color will be obtained. Dissolve this residue in 2 or 3 cc. of water, add a few drops of dilute HCl, and render faintly alkaline with solid sodium bicarbonate (avoiding an excess), shaking well after each addition. In the presence of morphine, codeine, apomorphine, heroine, or dionine, an emerald-green color is produced. If this mixture be shaken with a few cc. of ether, this latter solvent is colored red, while the aqueous layer remains green.

Fulton[2] has modified this test as follows: Put a little of the residue from the extraction process in a test tube and dissolve in a small amount of syrupy phosphoric acid (85 per cent.), and heat to boiling over a small free flame. Cool, dilute with a few cc. of water, and oxidize by adding several drops of iodic acid solution. An orange-red color is produced. Add considerable ammonium acetate, when the color changes through olive to bright green or blue-green. Ether extracts the red color characteristic of the oxidation product of apomorphine, while the aqueous layer is green.

5. *Ferric Chloride Test.*—This is one of the least delicate of the tests for morphine, but is of special value in that it differentiates morphine from codeine and heroine, with which morphine might be confused. A small portion of the dry residue is treated on a porcelain plate with a drop or two of *neutral* ferric chloride solution (1:20), when a blue color will appear in the presence of morphine or its salts. This reaction is by no means specific for morphine, but is, rather, merely a group reaction for the presence of a free hydroxyl group attached to the benzene ring. This reaction is given by oxydimorphine, but not with codeine or heroine, while

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[1] Jour. Lab. and Clin. Med., 1928, **13**, 750.

[2] *Loc. cit.*

with apomorphine the initial color is rose-red, which later changes to violet, and then to black.

6. *Iodic Acid Tests.*—There are two different and distinct iodic acid tests for morphine, one of which is in no way characteristic although very valuable in its negative phase as indicating the probable absence of morphine in the residue, while the other is rather distinctive of morphine.

If a portion of the dry residue be treated in a porcelain dish with a drop of dilute starch solution and evaporated to dryness, on moistening the cooled residue with a little of an aqueous solution of iodic acid a blue color will appear if morphine be present. This reaction is given by many reducing agents, especially important being extractive matters obtained from animal tissues, so that a positive reaction does not indicate the actual presence of morphine, although a negative test would be strong evidence that morphine was not present. If, now, the residue, whether or not a blue color has appeared, be treated with a few drops of ammonia water, a mahogany color appears in the presence of morphine (Lefort's test). This test is not given by codeine or heroine. Fulton recommends the addition of a few drops of hydrogen peroxide solution before the ammonia is added, a bright red color being produced instead of the brown.

Biologic Test.—It has been found by Straub and Herrmann[1] that white mice show a relatively characteristic response to injection of morphine or its salts. If a neutral or slightly alkaline (not acid) solution of morphine hydrochloride be injected under the skin of the back of a white mouse weighing about 16 to 20 grams (smaller animals are not suitable), the following symptoms are noted. The back of the animal assumes a lordotic curvature; the hind legs show a slight spastic paralysis, being more markedly stretched out than usual; movements of the animal appear difficult; the tail raises up in a characteristic S-shaped curvature, finally laying over the back of the animal with the tip being over the ear; the whole behavior of the mouse gives the impression of increased restlessness and stimulability, so that it springs into the air in response to slight noises, especially those of high pitch. There appears to be a direct relation between the continuance of the reaction and the amount of morphine injected. Thus, with a dose of 5 mg. the reaction continues about 20 hours, while with a dosage of 0.005 mg. it continues for 45 minutes. Likewise, the maximal reaction is related to the dosage. With a dose of 5 mg. the maximal response continues for 4½ hours, while with a dosage of 0.01 mg. this is 30 to 45 minutes. Papaverine, narcotine, narceine, thebaine, and ethylmorphine show this reaction somewhat irregularly and, even then, only in response to much larger doses than are necessary with morphine. Codeine, apomorphine, and heroine show similar reactions to morphine, but with the first two of these drugs the amount required to produce the reaction is 0.1 mg., while with heroine the response is shown by smaller doses, such as 0.005 mg.

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[1] Biochem. Ztschr., 1912, **39**, 216. See, also, Heinekamp, Jour. Pharm. and Exp. Therap., 1922, **20**, 107.

From the medicolegal standpoint this test is not sufficiently distinctive, by itself, to warrant a conclusion that morphine is present. It is, however, of value as a confirmatory test, and, also, as a preliminary procedure, as it is not absolutely necessary that the purification of the residue be carried further than the first stage to permit of the test being applied.[1]

Determination of Quantity.—Some estimation of the quantity of poison found in the tissues is, usually, desirable, in any case of poisoning, as only in this way may one be in a position to state whether or not a lethal dose was probably taken. Owing to the fact that with morphine, especially, the possibility of loss is very great, the figures obtained can be regarded as only approximate. Several methods have been advanced, but the simplest is the volumetric one. Measure out an aliquot part of the chloroform-alcohol extract, obtained from the purified material, and evaporate carefully at a very low temperature. Dissolve this dry residue in a known amount of N/10 sulphuric acid solution, and titrate the excess of acid with N/50 sodium hydroxide solution, using cochineal as an indicator. Each cubic centimeter of N/10 sulphuric acid combined with the morphine corresponds to 0.02853 gm. of anhydrous morphine.[2]

Detection of Codeine.—Codeine gives many of the reactions for morphine, such as the Pellagri and Husemann tests, while the color tones with Fröhde's and Marquis' tests are slightly different. Codeine is precipitated by solutions of caustic alkalies, and does not dissolve in excess as does morphine. Codeine does not give the iodic acid or ferric chloride tests. With Mecke's reagent (sulphuric acid containing 0.005 gm. of selenious acid per cc.)gives a green color, which changes rapidly to blue, then slowly back to green; while morphine with this reagent strikes a blue color, changing to green and then to brown.

Detection of Heroine.—Like codeine and morphine, heroine gives the reactions dependent upon conversion into apomorphine, such as Husemann's and Pellagri's tests. With Fröhde's reagent heroine shows a purple, which may gradually change to blue; while with Marquis' test the reddish tones may be more prominent with heroine than with morphine. Heroine does not reduce iodic acid, nor does it give a blue color with ferric chloride. If about 0.1 gram of heroine be heated with 1 cc. of alcohol and 1 cc. of concentrated sulphuric acid, the odor of ethyl acetate is recognizable, a test not given by either morphine or codeine.

[1] Tremonti, Boll. soc. ital, biol. sper., 1928, **3**, 393 (abstract in Chem. Abs., 1929, **23**, 477, has introduced a new biologic method, which is much more sensitive than the above, but is much more difficult of performance.

[2] See Lautenschläger, Arch. der. Pharm., 1919, **257**, 13, for a colorimetric method based on the formation of diazonium compounds; also, Gauss, Jour. Lab. and Clin. Med., 1921, 6, 699, for one based on the use of Marquis' reagent. Balls, Jour. Biol. Chem., 1927, 71, 543, uses silicotungstic acid for his gravimetric method. See, also Balls and Wolff, Ibid., 1928, **80**, 379.

On heating heroine with sulphuric acid and then adding a little chloral hydrate, a brownish-red color appears. Morphine gives with this test a violet color and codeine a bluish green, which gradually changes to red. If heroine be treated with a few drops of concentrated nitric acid, it dissolves with yellow color, which gradually, or immediately on heating, changes into a greenish-blue color, and finally becomes yellow (Zernik's reaction).

Owing to the ready hydrolysis of heroine, the alkaloid extracted from the tissues usually shows the reactions for morphine, rather than for heroine. McNally[1] has shown that the deacetylization of heroine does not take place in the stomach, so that we may recover this alkaloid, by proper methods, from the stomach and its contents, while the extracts from other organs will, probably, show only morphine. The method advocated by McNally is as follows: Extract the alkaloid from the tissue by successive portions of 50 per cent. alcohol acidified with a few drops of 10 per cent. tartaric acid. Keep the temperature of the samples close to 50°C. Allow the combined extractions to remain in a cool place until the fat separates. The fat is separated in a separatory funnel, washed with acidified water, and the washings added to the main extracts. If the sample is allowed to stand overnight, considerable extraneous material settles to the bottom of the flask and may be removed by filtration, washing the residue with 50 per cent. alcohol. Evaporate the alcoholic extracts under diminished pressure, the water-bath being kept well under the boiling-point. The pasty residue is taken up with a little cold acidified water, and the extraneous matter filtered off. The filtrate is allowed to filter into 95 per cent. alcohol, the protein substances and other impurities thus becoming granular on standing and capable of easy filtration. The alcohol is evaporated off under diminished pressure, until the liquid in the distilling flask amounts to about 20 cc. This residue is taken up with cold water, acidified with tartaric acid, and filtered. To the filtrate is added 1 gram of "alcresta" (Lloyd's reagent, see page 609), and the mixture well stirred. The alcresta, together with its adsorbed substances, is filtered off and the liquid tested for alkaloids by the usual precipitants. If any alkaloid remains in the filtrate, more alcresta is added and the mixture filtered. Transfer the alcresta containing the alkaloid to a separatory funnel, and extract with successive portions of ammoniacal chloroform. The chloroform is drawn off and evaporated, leaving the free alkaloid as a residue. The alkaloid may be weighed and then submitted to the tests for heroine mentioned above.

Detection of Ethyl Morphine (Dionine).—The reactions of dionine are much the same as those of codeine, although with Marquis' reagent dionine first strikes a definite green, then becomes blue and, finally, bluish-violet. If a drop of 10 per cent. ferric chloride solution be added to a solution of a small amount of dionine in 10 cc. of sulphuric acid, and warmed on the water-bath, the mixture will become at first green, then deep violet-blue, and, after the addition of a drop of nitric acid, deep red.

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[1] Jour. Lab. and Clin. Med., 1917, 2, 649.

Differentiation of Opium from Morphine.—As an important constituent opium containes meconic acid bound to some of the alkaloids. Hence, it follows that if both morphine and meconic acid be found in the analysis, the evidence of opium poisoning is complete. The most satisfactory material for examination for meconic acid is the stomach and its contents, although this has been found in the liver and kidneys. The extraction of meconic acid may be combined with that of the alkaloids, as this acid is withdrawn from acid solutions by amyl alcohol with difficulty, but readily with acetic ether. Or the process for extraction of alkaloids may be carried to the point of obtaining the acid aqueous solution, and this may be filtered and treated with lead acetate solution in slight excess. The precipitate may be examined for meconic acid, while the filtrate may be reserved for the detection of alkaloids. Suspend the precipitate of lead meconate in a little water, and treat with hydrogen sulphide to remove the lead. Filter, and concentrate the filtrate to a small volume, filtering again, if necessary to assure a clear solution. On treating this solution with ferric chloride solution, a brown-red to blood-red color is obtained. This color is not readily destroyed by boiling nor by hydrochloric acid (difference from acetic acid), nor by addition of mercuric chloride (difference from thiocyanic acid). The color is, however, destroyed by the addition of stannous chloride, but the color returns on addition of nitrous acid.

PHYSOSTIGMINE

This base, also called eserine, is the chief characteristic poisonous alkaloid of the Calabar bean (*Physostigma venenosum*), also known as the ordeal bean, the esere nut, or the chap nut. Either physostigmine itself, or a closely related alkaloid, is found, also, in the Cali nuts, the seeds of *Mucuna urens*. Other alkaloids, such as eseridine, eseramine, isophysostigmine, physovenine, and geneserine have been reported as present in this bean, but these latter alkaloids appear to have little, if any, toxicologic significance.

The Calabar bean, itself, is oblong or ellipsoidal, somewhat compressed reniform, from 15 to 30 mm. in length, and from 10 to 15 mm. in thickness; externally reddish or chocolate brown, smooth, somewhat wrinkled near the brownish-black groove, the latter being about 2 mm. in width and extending almost the entire length of the convex edge, and in which are frequently found the remains of the white, membranaceous funiculus, the margins of the seed-coat on both sides of the groove somewhat elevated, of a yellowish-red or brownish-red color and somewhat thickened; embryos large, white, with short hypocotyl and two concavoconvex cotyledons. The seeds should yield not less than 0.15 per cent. of the alkaloids of physostigma.

The only official preparation of physostigmine, under the present Pharmacopoeia, is the salicylate, the extract and tincture of the bean no longer being recognized.

The number of fatal cases of poisoning from physostigmine reported is very small, only two such cases being found in the literature. Attempts at suicide have been unsuccessfully made, while a large number of cases of actual nonfatal poisoning have occurred from eating the beans. Most of the cases of poisoning arise from overdoses as medicinal agents.

Properties.—Physostigmine is a monacid, tertiary base, with the chemical formula $C_{15}H_{21}N_3O_2$, its graphic structure being still unsettled. It forms crystals, which, when pure, are colorless, but often have a pale red tint. It is almost tasteless. It melts at 105° to 106°C. It is very slightly soluble in water, readily soluble in alcohol, ether, chloroform, benzene, and carbon disulphide, but insoluble in petroleum ether. It is levorotatory, and its solutions are strongly alkaline to litmus.

Physostigmine salicylate ($C_{15}H_{21}N_3O_2.C_7H_6O_3$) occurs in the form of colorless or faintly yellow, shining, odorless, crystals. It acquires a red tint when long exposed to light and air. As it is tasteless, great caution must be used in submitting a residue to the taste test, owing to the possibility of an overdose. One gram of the salt dissolves in 75 cc. of water, 16 cc. of alcohol, 6 cc. of chloroform, and in 250 cc. of ether at 25°C.; also in 16 cc. of water at 80°C., and in 5 cc. of boiling alcohol. Its cold-saturated aqueous solution is neutral or only faintly acid to litmus paper. Upon standing, the solution usually acquires a pink color, which is rapidly produced by the addition of a few drops of sodium hydroxide solution.

Symptoms.—In man physostigmine elicits practically the same results as noted experimentally in the dog, namely, vomiting and pain in the stomach, dyspnea, giddiness, and muscular weakness, contraction of the pupil, salivation, and perspiration. The respiration is at first rapid and deep, and later slow and dyspneic; the heart is slow; muscular twitching may be present, and complete collapse may follow. The drug has, apparently both a central and peripheral action, the former being shown in the paralysis of the brain and cord, after a primary stimulation; while the peripheral action is indicated in the stimulation of the striped musculature and the glands leading to oversecretion, excessive mucous secretion, and stimulation of peristalsis. While the pupils are ordinarily contracted by physostigmine, this is not a uniform finding, as dilatation may be noted, as in the case reported by Leibholz.[1]

Fatal Dose.—It is a very difficult matter to state the probable fatal dose of this alkaloid, as only two reports of death are found in the literature. Cloetta[2] and Rost[3] both give the minimum lethal dose as 0.01 gram. In one of the fatal cases, death followed in a very short time after the eating of six of the beans, while the dose in the other case is indefinite. Quite a few cases of toxic action have been reported from the use of the drug in ophthalmology from varying dosages, absorption taking place from the mucous membrane, while Leibholz[1] reports the attempted suicide of two women from a dosage of 0.1 gram of the sulphate.

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[1] Vrtljschr. f. ger. Med., 1892, 3 F., **3**, 284.

[2] *Lehrbuch der Toxikologie* by Flury and Zangger, 1928, p. 293.

[3] *Toxikologie* by Starkenstein, Rost and Pohl, 1929, p. 430.

Treatment.—The physiologic antidote is atropine given subcutaneously in doses of 0.5 to 1 mg. In case cerebral excitement is present, Kobert advises the use of scopolamine instead. Later the depression is treated by administration of camphor, caffeine, and strychnine, the latter to be used cautiously.

Postmortem Appearances.—The autopsy findings show little that is characteristic. In Kratter's[2] case, which is the only one reported in which an autopsy was made, the findings were hyperemia of the brain and its coverings; evidences of stimulation of the mucous membrane of the stomach and duodenum; hypervenosity of the blood and its accumulation in the lungs, heart, and large vessels; subpleural ecchymoses; and marked narrowing of the large intestine.

Detection.—Physostigmine is somewhat quickly eliminated by the urine, bile (feces), saliva, and milk. Some of it is, undoubtedly, decomposed in the system, but it appears to be fairly well distributed throughout the organs, as shown by the examination of a fatal case by Kratter. Although somewhat easily decomposed by strong bases, physostigmine seems to be quite resistant to putrefaction as Kratter allowed the organs in his fatal case to putrefy for 7 months and was able to detect the alkaloid, while Pellacani[3] permitted physostigmine to remain in contact with putrefying blood for 7 months, after which he easily detected the alkaloid.

In extracting physostigmine from the tissues, every precaution should be exercised to prevent decomposition. The alkaloid may be recovered by the usual process for alkaloids, the original acid-alcohol extraction being, preferably, made at room temperature, and the alcohol removed by distillation *in vacuo*. Sodium bicarbonate should be used for alkalinization, and either ether or benzene, or, as recommended by Kratter, chloroform, followed by alcohol-containing chloroform, and, later by chloroform-ether, as the immiscible solvent. In this process it is to be noted that the acid extract of the organs has a peculiar red-brown color, which becomes clear red on alkalinization, due to the formation of rubreserine.

Chemical Tests.—1. *Rubreserine Test.*—On exposure to air and light, an aqueous solution of eserine becomes red, and ultimately dark brown with formation of a red crystallizable coloring-matter called rubreserine. On treating this red solution with a reducing agent, such as hypophosphorous acid, sulphurous acid, hydrogen sulphide, sodium thiosulphate, or nascent hydrogen in the presence of free acid, the liquid is decolorized.

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[1] *Loc. cit.*

[2] Vrtljschr. f. ger. Med., 1912, 3F., **43**, II Supp., 262.

[3] Virchow's Jahrb., 1885, **1**, 530.

If the colorless aqueous solution be shaken for some time with an excess of potassium or sodium hydroxide, it rapidly acquires a pink tint. On agitating with chloroform, the rubreserine is dissolved out and colors the chloroform orange-red.

2. *Ammonia Test.*—If a small amount of the residue obtained in the extraction process be treated with an excess of ammonia and evaporated to dryness on the water-bath, it turns in succession pale red, red, yellowish-red, green, and finally blue, this latter residue being known as eserine blue. This dissolves in alcohol with a blue color. Excess of dilute acetic or mineral acid added to this solution causes a change in color to litmus-violet, if viewed by transmitted light, or to red, if examined by reflected light, showing at the same time a strong eosin-red fluorescence. If again made alkaline with ammonia, chloroform will dissolve the dyestuff with a green-blue color. Examined spectroscopically, the blue alkaline solution shows one absorption band in the red, while the red acid solution exhibits one absorption band in the yellow. On treating the blue solution with reducing agents, the solution first becomes red and is, then, decolorized.

3. *Nitric Acid Test.*—If an aqueous solution of the suspected residue be heated to boiling, and a few drops of concentrated nitric acid be added, an orange colored liquid is obtained, which, on addition of an excess of sodium hydroxide, turns intensely violet if physostigmine be present.

Biologic Test.—If two or three drops of a dilute neutral solution of the alkaloidal residue be dropped in the conjunctival sack of the cat, contraction of the pupil will, usually, be shown within 20 minutes. This test is given by 0.005 to 0.01 mg., and rarely fails, although all cases of poisoning may not show this myosis as a clinical sign.

STRYCHNINE AND NUX VOMICA

Many species of Strychnos, a genus of plants of the order *Loganiaceae*, contain strychnine and brucine, the former of which is of special importance in toxicology. These two alkaloids occur principally in the seeds of *Strychnos nux vomica* and of *Strychnos ignatii* (St. Ignatius' bean), in the wood of *Strychnos colubrina*, in the root-bark of *Strychnos tieuté* (the deadly upas tree, upas tieuté, or upas Radja). The leaves of *Strychnos nux vomica* contain brucine but no strychnine, while the root of *Strychnos icaja* contains strychnine, but no brucine. Neither strychnine nor brucine are found in the seeds of Strychnos *potatorum*, *brachia*, *innocua*, *pseudoquina*, *spinosa*, *laurina*, or *monosperma*, while the bark of *Strychnos castelnaei*, *toxifera*, or *Crevauxii* is the common source of curare (curarine).

The official preparations of nux vomica are the seeds themselves, the extract, yielding not less than 15.2 per cent, nor more than 16.8 per cent of the alkaloids of nux vomica, and the tincture, 100 cc. of which yield not less than 0.237 gram, nor more than 0.263 gram of the alkaloids of nux vomica. The official alkaloidal salts are strychnine sulphate and nitrate.

While the U. S. Pharmacopoeia directs that the ripe seeds of *Strychnos nux vomica* shall yield not less than 2.5 per cent. of the alkaloids of nux vomica, and shall be used as the source of the official preparations, it is to be said that brucine predominates over strychnine in this species, while in *Strychnos ignatii* a mere trace of brucine is found, while the strychnine contents is about 1.5 per cent.

Cases of strychnine poisoning have been relatively numerous in past years, the majority of these, apparently, being of a suicidal nature. In 1856 Husemann collected 92 cases, Schauenstein 200 cases up to 1868, Falck 57 cases for the years 1869-1880, and Koppel 116 cases from 1880 to 1889.[1] In 1911 Witthaus collated 663 cases of strychnine poisoning, of which 313 (47.3 per cent.) were suicidal; 189 (28.5 per cent.) were accidental; 134 (20.1 per cent.) homicidal; and 27 (4.1 per cent.) were of unknown type.[2] In the years 1909 to 1913 the suicidal cases in Germany ran from 11 to 19 per year.[3] According to the U. S. Census Report for the 1910 Census[4] strychnine poisoning was the cause of death 210 times, 113 cases suicidal, and 97 accidental. The cases, however, seem to be getting less frequent, the suicidal cases in New York City for instance in the years 1925–1927 being only 3.[5] It is to be remembered that many cases of poisoning do not find their way into the literature, being reported only in court records, or not investigated at all.

Properties.—Strychnine was discovered in 1818 by Pelletier and Caventou. Its chemical formula is $C_{21}H_{22}N_2O_2$, but, in spite of the large amount of work upon it, the structural formula is still unsettled. Strychnine is a monacid, tertiary base combining with one equivalent of acid to form salts. It is believed to be an inner anyhydride of an imino-carboxylic acid (strychnic acid), which appears to contain 2 carboxyl groups, one of which is neutralized by the basic nitrogen, while the other gives to strychnine its acid character. It occurs in colorless, transparent, prismatic crystals of the rhombic system, or as a white crystalline powder; odorless and permanent in the air. It is very markedly bitter, this being manifest in very dilute solutions. One gram of strychnine dissolves in 6420 cc. of water, 136 cc. of alcohol, 5 cc. of chloroform, and in 180 cc. of benzene at 25°C.; also in 3100 cc. of boiling water, and in 34 cc. of boiling alcohol; very slightly soluble in ether. Its saturated solutions are alkaline to litmus and are levorotatory. It is precipitated from solutions of its salts by the general alkaloidal reagents, picrolonic acid being especially valuable for this purpose. It is, also, precipitated by the fixed alkali hydroxides and carbonates, and is not readily soluble in excess of these reagents, although ammonia, when it is in excess, may dissolve it to some extent. Even bicarbonates may slowly precipitate strychnine, so that prescriptions containing these elements may throw down strychnine, and the consumer may get a toxic dose by taking the residue in the bottle.

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[1] See Kobert, *Lehrbuch der Intoxikationen*, 2te. Aufl., 1906, **2**, 1154.

[2] *Toxicology*, 1911, p. 1015

[3] See *Toxikologie* by Starkenstein, Rost and Pohl, 1929, p. 48.

[4] See Wilbert, Pub. Health Reports, No. 330, 1916.

[5] See Report of the Chief Medical Examiner of the City of New York, 1925–27.

Strychnine Nitrate ($C_{21}H_{22}N_2O_2HNO_3$).—This official salt occurs in colorless, glistening needles, or as a white, crystalline powder; odorless, and permanent in the air. Even very dilute solutions are intensely and persistently bitter. One gram of strychnine nitrate dissolves in 45 cc. of water, 150 cc. of alcohol, 50 cc. of glycerin, and in 105 cc. of chloroform at 25°C.; also in 10 cc. of boiling water, and in 80 cc. of alcohol at 60°C.; insoluble in ether. Its aqueous solution is neutral or only slightly acid to litmus, and is levorotatory.

Strychnine Sulphate ($(C_{21}H_{22}N_2O_2)_2H_2SO_4.5H_2O$).—This official salt occurs in colorless or white prismatic crystals, or as a white crystalline powder; intensely bitter, odorless, and efflorescent in dry air. One gram of the salt dissolves in 35 cc. of water, in 81 cc. of alcohol, and in 220 cc. of chloroform at 25°C.; also, in 7 cc. of boiling water, and in 26 cc. of alcohol at 60°C.; freely soluble in glycerin; insoluble in ether. Its aqueous solution is neutral or only slightly acid to litmus and is levorotatory.

Brucine ($C_{23}H_{26}N_2O_4$).—Brucine is a monacid, tertiary base, and is a dimethoxy derivative of strychnine. It occurs as a bitter, white, odorless, crystalline powder, or as colorless, transparent, monoclinic prisms or shining leaflets, containing 2 or 4 molecules of water of crystallization. It forms readily crystallizable soluble salts. Brucine is more readily soluble than strychnine in both water and in alcohol. It is readily soluble in acetone, benzene, chloroform, and amyl alcohol; while it dissolves in ordinary ether, it is almost insoluble in absolute ether, and difficultly soluble in petroleum ether. Its solutions show a marked alkaline reaction and are levogyrate.

Symptoms.—When the poisoning arises from strychnine or nux vomica taken by the oral route, the symptoms begin in many cases in 10 to 15 minutes after the ingestion of the poison, but they have been known to begin immediately, and, in other cases, they may be delayed for an hour and even longer, there being in such cases an initial period of nervous excitation without violent symptoms. If a toxic dose is given hypodermically, the action is manifest promptly. Usually, the first symptoms are a sense of tightness of the chest, stiffness of the neck, slight shudderings, and a feeling of impending calamity, drawing of the hands and feet, and, ere long, quite a sudden and violent tetanic convulsion, in which there are extension of the legs, arching of the feet, with the head drawn back, sometimes to such an extent that the body rests upon the heels and the back of the head (opisthotonos, which may be replaced by emprosthotonos or by pleurosthotonos), the arms extended or drawn tightly across the chest, the face fixed in a grin (*risus sardonicus*), the eyes staring, and the muscles of respiration so stiffened that suffocation seems imminent. During the attack, the pulse is weak and irregular, the countenance is livid, the pupils are dilated, and, not infrequently, foam appears at the mouth. The convulsion may last from ½ minute to several minutes; while the interval between convulsions is from a few minutes to ½ hour. The number of spasms varies from 1 to 10, but death may occur during the first convulsion. In the interval between convulsions, the muscular rigidity may completely disappear, there is general relaxation, a cold perspiration covers the surface of the body, and there are contraction of the pupils and a sense of weariness. The patient sometimes falls asleep, but is sent into another convulsion by any sudden movements in the room or by sounds outside. The mind is clear, as a rule, up to the end, but may be somewhat dulled during the paroxysm. According to Stewart and Rogoff[1], strychnine markedly increases the amount of epinephrine secreted by the suprarenal glands, and, consequently, causes an increase in the amount in the blood, this increase of epinephrine bringing about an increase in the total number of leucocytes, both lymphocytes and polymorphonuclears.[2]

The above symptoms are so distinctive, when they run an ordinary course and have been carefully observed, that they may be, ordinarily, relied upon for a diagnosis of the type of poisoning. While chorea, epilepsy, uremic and puerperal convulsions have been claimed to present symptoms apt to be mistaken for strychnine poisoning, yet there are so many factors that obtain in these diseases, that are not present in strychnine poisoning, that they could hardly be confused with poisoning. Tetanus, however, may at times closely resemble strychnine poisoning, so that the history of the case should be carefully studied before arriving at an absolute diagnosis based on symptomatology alone. In both, there are violent tonic convulsions, which are very similar, but in other respects these conditions differ considerably. In tetanus there is a history, if such can be obtained, of an injury, and the disease comes on gradually and progresses slowly to a fatal termination; while in strychnine poisoning there is no antecedent injury and the manifestations appear suddenly and progress rapidly to the fatal outcome. In tetanus the muscles first affected are, generally, those of the back of the neck, and those of the jaw are early involved producing persistent lockjaw; while in strychnine poisoning, either the muscles of the extremities are first affected, and those of the neck and jaw last attacked, or the entire muscular system is involved almost simultaneously. Between spasms, the muscular rigidity is prone to persist to some extent in tetanus; while in strychnine poisoning there is almost always complete relaxation. Of course, in both conditions exceptions may occur, so that the diagnosis may, in some cases, be somewhat difficult.[3]

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[1] Jour. Pharm. and Exp. Therap., 1919, **13**, 95; Ibid., 1920, **16**, 71; and Ibid., 1921, **17**, 227.

[2] See Edmunds and Lloyd, Jour. Lab. and Clin. Med., 1923, **8**, 563.

[3] See Haines, Hamilton's *System of Legal Medicine*, 1894, **1**, 449.

The symptoms following administration of *brucine* resemble somewhat those of strychnine, although they are much weaker, from 30 to 40 times as large a dose of brucine being required to produce the same effect. The convulsive seizures may not appear under the action of brucine. In the only authentic case of brucine poisoning found in the literature, this being non-fatal, 2 grains of brucine produced essentially the symptoms of strychnine poisoning, but the convulsions were not so severe, recovery being rapid.[1]

Fatal Dose.—The smallest fatal dose of strychnine, as far as we have found, is 0.016 gram (¼ grain) reported to have caused the death of a woman of 36 years in 1¾ hours.[2] In two cases, accurately fixed doses of 0.032 gram (½ grain) have caused death, one in which a woman of 22 years of age died in 5 hours, the other the case of Dr. Warner, who died in 14 minutes.[3] Several deaths have been reported from about ¾ grain[4], and, also, from 1 grain.[5] Although the above-mentioned doses have caused death, the *average fatal dose* of strychnine for man, following internal administration, is 0.1 to 0.12 gram (1½ or 1¾ grains). Recovery has, however, been reported from doses of 9, 15, 19, 20, 27, 32, and 40 grains.

Fatal Period.—In the majority of fatal cases death occurs in from 1 to 3 hours, although cases of death in 10 minutes and in 15 minutes have been reported. According to Witthaus[6], "In 92 of 186 fatal cases in the reports of which the duration is stated, it was less than one hour, in 44 it was from one to two hours, in 14 from two to three hours, in 14 from three to four hours, and in 22 longer than four hours." If life is prolonged for 5 or 6 hours, recovery is probable.

Treatment.—The stomach should be washed out as quickly as possible, finely powdered charcoal, solution of iodine (15 drops of the tincture in ½ glass of water), potassium permanganate (¼ teaspoonful of the crystals dissolved in a pint of warm water), or tannic acid being added to the wash water. In some cases the stomach tube can not be passed owing to the rapid appearance of convulsions, so that it may be necessary to precede the gastric lavage by inhalation of ether or chloroform to quiet the patient. The convulsions may be controlled by these anesthetics, while chloral hydrate, by mouth or by rectum, or other narcotics should be given during the intervals between spasms. The patient should be kept as quiet as possible, as any sudden stimulus, noise, or even a draft of air, may bring on a paroxysm. If respiration becomes markedly embarrassed artificial respiration may be necessary, probably with inhalation of pure oxygen. If the patient can be carried through the early periods, recovery will probably follow.

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[1] Sozinskey, Med. and Surg. Reporter, 1882, **47,** 194.

[2] Medical Times and Gaz., 1854, **8** (n. s.), 376.

[3] Jones, Lancet, 1856, **2,** 291 and 302; Boston Med. and Surg. Jour., 1847, **36,** 209.

[4] See Watson, Lancet, 1846, **1,** 73; Ogston, Ibid., 1856, **1,** 428; Socquet, Ogier, and Balthazard, Ann. d'hgy., 1907, 4 s., **7,** 523.

[5] See De Courcillon, Med. Arch., 1869, **3,** 31; and Dill, Lancet, 1873, **2,** 533.

[6] *Toxicology,* 1911, p. 1031.

Postmortem Appearances.—Almost immediately after death intense rigor mortis may set in, or, even, this may be practically continuous with the rigidity shown during the convulsions, so that there may be no period of flaccidity between a terminal spasm and the rigor mortis. The joints are fixed, the fingers clenched, the feet arched, and, sometimes, opisthotonos obtains. This rigidity continues for a variable time, occasionally even for a week. Beyond this finding, there is little else characteristic. The internal organs show the usual signs of asphyxia, the brain and upper portions of the spinal cord, with their membranes, usually, show congestion, the same conditions frequently being observed in the liver and kidneys. The heart varies in respect to the amount of blood it retains.

Detection.—As absorption of strychnine from the gastro-intestinal tract is not especially rapid, it is to be expected that considerable of the alkaloid ingested will be found in the stomach, and less in the intestines. Salant believes that the alkaloid in the intestines changes to such an extent that it is hardly recognizable by chemical tests. While this may be true in experimental animals, the writer has found strychnine in the feces in several cases, possibly arising from excretion through the bile. Elimination of strychnine takes place mainly through the urine, and, to a less extent, through the perspiration, saliva, bile, and milk, and not at all by the feces, according to Hatcher and Eggleston.[1]

It is, probably, true that much of the strychnine is destroyed in the system, so that such organs as the liver[2], kidneys, and brain may contain only very small amounts of the alkaloid, unless death is relatively rapid. Indeed, there are quite a few cases of death from undoubted strychnine poisoning, in which competent chemists have been unable to find strychnine. Thus, Haines[3] states that he examined the stomachs of two children, who died suddenly with all of the symptoms of strychnine poisoning, but could not obtain any indication of the poison in either case. On the other hand, there are cases in which strychnine is found in the organs in small amount as a result of therapeutic administration. The analyst must, therefore, be on his guard in arriving at conclusions, without some knowledge of the history of the case and some idea as to the possible remedial use of strychnine.

In spite of its ready decomposition in the body during life, strychnine resists decomposition in the cadaver for long periods. Cram and Meserve[4] found strychnine in the liver and spinal cord of a cadaver exhumed after 4 months; Haines[5] extracted it in ponderable quantity from a body buried for nearly 12 months; Allen[1] recovered it from a stomach that had been preserved in alcohol for 6 years; Lesser[2] detected it in the completely mummified body of a woman 337 days after death; while Kratter[3] discovered it in the body of a man buried for 5 years and 8 months, which had been externally converted into adipocere.

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[1] Jour. Pharm. and Exp. Therap., 1917, **9**, 359.

[2] See Weiss and Hatcher, Ibid., 1922, **19**, 419.

[3] Hamilton's *System of Legal Medicine*, 1894, **1**, 459.

[4] Jour. Biol. Chem., 1910, **8**, 495.

[5] Hamilton's *System of Legal Medicine*, 1894, **1**, 459.

As is the case with many other alkaloids, certain putrefactive bases have been confused, in some cases, with strychnine, and mistakes of identity have been reported. In none of these cases, however, should mistakes have occurred, if the totality of identifying tests were considered. It is to be emphasized that no single test should be taken as the basis of an unequivocal report as to the identity of a residue, but that exact similarity in all respects should be present, if the color reactions are to be properly interpreted. Unless chemical and biologic tests agree, strychnine cannot be definitely proven to be present.

The usual process for separation of the alkaloids from tissues may be utilized in extracting strychnine. Alkalinization should be affected with ammonia, and chloroform should be employed as the immiscible solvent. Should annoying emulsions form on shaking with chloroform, an equal volume of ether may be added, and the ether-chloroform solvent may be used in the second and third extractions, but chloroform alone is to be preferred, if it does not form too strong an emulsion. The residue obtained by the usual process is, often, impure, so that resort is made, for the purpose of purification, to the following method. Moisten the dry residue, obtained by evaporation of the chloroform solvent, with 2 or 3 drops of concentrated sulphuric acid, and heat the mixture on the water-bath for an hour or two, or to 120°C. for 15 or 20 minutes in the drying oven. Allow to cool, stir the carbonized residue with water, filter, wash, make faintly alkaline with ammonia, and shake out with chloroform. Concentrate the chloroform extract to some extent and preserve in a small graduated stoppered cylinder. Small portions of this purified extract are taken for the qualitative tests. This treatment with sulphuric acid destroys most other alkaloids, and, especially, ptomaines, if present, so that there should be no confusion of reactions when working with such a purified extract.

Chemical Tests.—The tests for strychnine are quite distinctive, especially when applied to the purified residue. Its ready capability of crystallization and its bitter taste should be of great preliminary value in distinguishing it from putrefactive bases. The bitterness of strychnine is, possibly, more intense and more persistent than that of almost any other known substance. While individuals differ in their ability to distinguish bitterness, yet one who is specially sensitive may perceive the bitterness in a solution diluted to 600,000 to 700,000 parts, while the ordinary person should have little difficulty with a 1:100,000 or, at least, a 1:50,000 solution. Absence of a bitter taste of an isolated residue is almost absolute evidence of the absence of strychnine, provided the person making the test is able to detect a bitter taste.

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[1] *Commercial Organic Analysis*, 1912, **6**, 459.

[2] Vrtljschr. f. ger. Med., 1898, 3 F., **15**, 270.

[3] Vrtljschr. f. ger. Med., 1907, 3 F., **33**, 131.

1. *The Fading Purple Test.*—A film of residue, obtained by evaporating a few drops of the chloroform solution on a white porcelain surface, is treated with a drop of concentrated sulphuric acid and allowed to stand for a short time to dissolve. No color is given by the sulphuric acid alone. If, now, a small crystal of potassium dichromate is slowly drawn through this solution by means of a glass rod, an evanescent play of colors will be observed, first a momentary blue, changing to deep violet, then to purplish-red, cherry red, and finally to orange or yellow. In the presence of small amounts of strychnine this play of colors may be very rapid, while with larger amounts the purple tints may persist for some time before the fading colors are noted. Care should be taken not to leave the dichromate in contact with the acid for a long period, as there may be some confusion in the coloration. The analyst should make himself familiar with the behavior of the oxidizing agent with sulphuric acid alone and with the sulphuric acid solution of strychnine, before pronouncing the identity of the residue. Occasionally, there may be some darkening when the sulphuric acid is added to the strychnine, due to the presence of impurities, but, if this is not marked, the darkening may be disregarded. Properly purified residues will show no change in color on the addition of the acid. Instead of using the dichromate as an oxidizing agent, some workers prefer others, such as potassium ferricyanide, cerosoceric oxide, manganese dioxide, lead peroxide, or potassium permanganate, but the writer prefers the dichromate or cerosoceric oxide.

The fading purple test is prevented, or at least obscured, by the presence of much brucine (which may possibly be present in cases of nux vomica poisoning) or by much morphine. If the residue be purified with hot sulphuric acid, as previously directed, these two alkaloids will be oxidized, while strychnine is unaffected. Should the residue, however, contain both strychnine and brucine, dissolve it in about 2 cc. of dilute sulphuric acid, add 2 drops of concentrated nitric acid, and let the mixture stand 3 or 4 hours. Render this mixture alkaline with sodium hydroxide and extract thoroughly with ether. On evaporating the ether, the residue will be practically brucine-free, as ether does not remove the oxidation products of brucine. On testing this residue with the above fading purple test, the results are quite satisfactory.

2. *Mandelin's Test.*—This test is essentially the same as the above, except that the reagent is added in one step instead of the two as above described. On adding to a small portion of the dry residue from the chloroform evaporation a drop or two of Mandelin's reagent[1], a deep violet-blue color appears, changing to a deep purple, and then to a cherry red, becoming yellow only on long standing. The color change with

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[1] A 1 per cent. solution of ammonium vanadate in concentrated sulphuric acid.

this reagent is much slower than with the other oxidizing agents, with the possible exception of cerosoceric oxide, so that this test is to be especially recommended.

3. *The Chromate Test.*—Evaporate a few drops of the chloroform solution, obtained in the extraction process, upon a glass slide. Take up the residue with a drop of dilute acetic acid, and allow most of the acid to dissipate. Now add a drop of an aqueous solution of potassium dichromate and stir carefully. Gradually, crystals will appear in the form of a yellow crystalline deposit of octahedral and dendroidal forms, the former being the more distinctive, although the latter are, perhaps, more frequently obtained. On touching this crystalline deposit with a drop of concentrated sulphuric acid, the fading purple test is obtained, just as in the direct color test.

4. *Malaquin's Test.*—Dissolve a small portion of the residue, obtained by evaporation of the chloroform solution, in a little dilute hydrochloric acid and mix with 2 cc. of concentrated hydrochloric acid and 1 gram of pure granulated zinc. After allowing to stand for 2 or 3 minutes, heat quickly to boiling and allow to cool. Now overlay carefully concentrated sulphuric acid with the above solution, when a rose-red ring will be formed at the point of contact of the two liquids, if strychnine be present, and gradually the whole mixture becomes rose red. This color is destroyed by the addition of a solution of potassium sulphocyanate, ammonia, or sodium hydrogen sulphate in excess. According to Malaquin[1] this test will detect strychnine in a dilution of 1 to a million. The only known alkaloid, which might be mistaken for strychnine by this test, is said to be veratrine, but this is differentiated by boiling the rose-red solution, when the red coloration with veratrine is changed to a dirty yellow, while that with strychnine remains unchanged.

Biologic Test.—Evaporate several drops of the chloroform solution to dryness and dissolve this in a few cc. of very dilute acetic or hydrochloric acid. Evaporate this acid solution to dryness and dissolve the residue in about 1 cc. of distilled water. Select a lively frog, and inject the above solution into the lymph-sac immediately beneath the skin of the back at the root of the hind legs. Note the time, and place the frog in a large loosely covered beaker, or under a bell-jar. Toxic symptoms will appear in 5 to 30 minutes, depending upon the amount of strychnine injected. The reflex irritability of the animal is much increased, especially to tactical, optical, and acoustic stimuli. As the toxic action develops, the animal shows a period of uneasiness with accelerated respiration, and, following this, the characteristic tetanic spasms appear, the hind legs being extended. At first the convulsions are of short duration, and the animal may draw up their hind legs during the remission. Later the spasms become more frequent, and the legs are kept extended. The return of the convulsions is hastened or brought about by tapping on the table, by changing the intensity of the light, or by touching the animal. This test is given by doses of 0.02 to 0.05 mg., when medium sized frogs are used.[1]

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[1] Jour. Pharm. et Chim., 1909, 6eme S., **30**, 546.

Determination of Quantity.—It is to be understood that no alkaloid can be separated from the tissues without loss, so that the figures obtained are only approximate. Evaporate an aliquot part of the chloroform solution to dryness, and dissolve this dry residue in a known amount of N/10 sulphuric acid solution. Titrate the excess of acid with N/50 sodium hydroxide solution, using cochineal or methyl red as indicators. Each cc. of N/10 sulphuric acid combined with the alkaloid corresponds to 0.03343 gram of strychnine.

Chemical Tests for Brucine.—Although there have been no fatal cases of brucine poisoning reported in the literature, yet it is sometimes necessary to show the presence of brucine in the residues extracted from the tissues, in order to prove a case of nux vomica poisoning in contradistinction to one arising from strychnine alone. As brucine is removed from aqueous alkaline solutions by ether or chloroform, this alkaloid may be found along with strychnine, and may be separated from it by the method given on page 690, or a combination of the tests for brucine and strychnine may be made with the same residue, as outlined below.

1. *Nitric Acid Test.*—To a portion of the residue obtained by the evaporation of the original chloroform extract (not heated with sulphuric acid) on a white porcelain surface, add a drop of concentrated sulphuric acid. With this neither brucine nor strychnine give a color. On now adding to this solution a drop or two of concentrated nitric acid, a blood-red color is produced in the presence of brucine. Instead of using the mixture of acids, the residue may be treated directly with the nitric acid, when a blood-red color appears, changing to reddish-yellow, and, finally, to pure yellow in the presence of brucine. If a few drops of a freshly prepared dilute solution of stannous chloride in hydrochloric acid, or of colorless ammonium sulphide, be now added to the yellow solution, an intense purple color appears. This color is destroyed by excess of nitric acid, so that the smaller the quantity of this acid added, the more likely is the test to succeed.

If brucine has been shown in this test, the presence of strychnine may be, also, indicated, by drawing a small crystal of potassium dichromate through the yellow solution of the alkaloid in the mixed sulphuric and nitric acids, when the mixture will show the fading purple test as outlined above, as the interfering action of brucine on this test is removed by its oxidation.

Blyth's Test.—If the suspected residue be dissolved in strong alcohol and a little methyl iodide be added, in a few minutes circular rosettes of crystal groups appear, which are composed of methyl brucine iodide. A solution of strychnine in alcoholic solution gives no such reaction with methyl iodide, nor does the presence of strychnine interfere with this test for brucine.

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[1] This test is known under the name of Marshall Hall, who first suggested its use in forensic medicine. See Lancet, 1856, **1**, 36 and 335.

THE VERATRUM ALKALOIDS

The several species of Veratrum contain a number of similar alkaloids, whose chemistry and relations have been much confused, and are still more or less obscure. Thus *Veratrum Sabadilla*, also known as *Schoenocaulon officinale* or *Asagroea officinalis*, has yielded cevadine, veratridine, cevadilline, sabadine, and sabadinine, while *Veratrum Album* (white hellebore) contains jervine, pseudojervine, rubijervine, protoveratrine, and protoveratridine, and *Veratrum Viride* (green or American hellebore) contains essentially the same alkaloids as does white hellebore. The so-called "veratrine", which was formerly official, is a mixture of various alkaloids and is of variable quality and physiologic activity.[1] At the present time the only official preparations of veratrum are the dried rhizome and roots of *Veratrum viride* and the tincture made from this plant.

Poisonings by the alkaloids of veratrum are not very frequent, Witthaus[2] finding only reports of 33 cases in the literature, almost all of them being accidental.

"Veratrine", formerly official, is a mixture of the alkaloids from the seed of *Asagroea officinalis*. It is a white or grayish-white amorphous powder, odorless, but causing intense irritation and sneezing when even a minute quantity reaches the nasal mucous membrane. It is slightly hygroscopic. One gram of veratrine dissolves in 1700 cc. of water, 2.8 cc. of alcohol, 0.7 cc. of chloroform, and in 4.2 cc. of ether at 25°C.; also in 1345 cc. of water at 80°C.; insoluble in petroleum benzine. Its alcoholic solution is alkaline to litmus paper.

Symptoms.—The toxic principles of the various species of veratrum are cevadine and protoveratrine. The symptoms of poisoning usually appear within a few (twenty) minutes, but may be delayed for an hour or more. These are referable both to the action of the alkaloids on the terminations of the motor, sensory, and secretory nerves and to the action on the central nervous system, both of which actions resemble somewhat those noted after aconitine poisoning.

The symptoms begin with prickling and burning in the mouth, followed by a sensation of warmth and intense burning pain in the stomach. There is great thirst, and the patient has difficulty in swallowing. Then follow salivation, marked nausea and severe vomiting, violent purging, accompanied by tenesmus, and severe abdominal colic. The prickling sensations soon extend from the mouth and throat to the skin, which becomes reddened and is affected with an intense itching, followed by a profuse perspiration. Sneezing, lacrimation, and coryza may appear, but are not constant. The patient is restless and gradually becomes prostrated. The extremities are cold, vertigo may appear, and the pupil is dilated. Respiration becomes gasping, shallow, and superficial, severe dyspnea not being uncommon. The pulse is slow and irregular at first, due to vagus stimulation, but later becomes feeble, small, thready, and rapid, owing to vagus paralysis, a coincident lowering of the blood pressure being noted, although Pilcher and Sollmann[1] show that the alkaloids of veratrum have little or no effect on the vasomotor center. Death is usually due to respiratory failure, although it may occur from collapse due to cardiac weakness or to exhaustion from continuous vomiting.

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[1] For descriptions of these various alkaloids see *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 592 et seq.

[2] *Toxicology*, 1911, p. 1074.

Fatal Dose.—The fatal quantity of the drug is difficult to estimate. In 2 of the 3 reported veratrine poisonings, 0.2 and 0.3 gram were not fatal, while the third case, in which 1.9 grams of mixed alkaloids were taken in alcohol, death did not result. Outside of these, Witthaus was able to find reference to but six fatal cases, and these were from the tincture and not the alkaloids themselves, a teaspoonful proving fatal in 2 of the cases. Death may occur in less than an hour, but it is usually delayed for 2 to 5 hours, or even for 24 hours or longer.

Treatment.—Gastric lavage should be thoroughly carried out, after which the patient should be kept flat on his back, with the head somewhat lower than his feet, and vomiting should be restrained as much as possible. Warm applications should be applied to the feet, and stimulants, such as whiskey, strychnine and, if indicated, digitalis should be administered. To combat the impending failure of respiration, artificial respiration may be necessary.

Postmortem Appearances.—These are neither distinctive nor uniform, but, usually, include congestion of the stomach and bowels, and, sometimes, hyperemia of the brain and its membranes.

Detection.—The alkaloids of veratrum are extracted from the tissues by the usual process for alkaloids, ammonia being used for alkalinization, and ether or chloroform selected as the immiscible solvent, it being remembered that these solvents may extract the veratrum alkaloids to some extent from acid solutions. The residue obtained in such cases is, ordinarily, a mixture of the alkaloids. As these bodies are difficultly separable, the toxicologic tests employed are those for the mixed veratrum alkaloids.

1. *Concentrated Sulphuric Acid Test.*—If a few drops of concentrated sulphuric acid be placed upon a portion of the residue obtained in the extraction process, an intense yellow color will appear, and the residue will dissolve to a yellow solution, which soon changes to an orange shade with a strong greenish fluorescence, shown by reflected light, especially if the alkaloids be present in appreciable quantity. On standing the orange solution gradually changes to a blood-red and then to a deep carmine-red color, which persists for some hours. If the residue and acid be heated at once, on addition of the acid, the carmine-red color appears almost immediately, the persistence of this red color being quite characteristic of the veratrum alkaloids. If Fröhde's,

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[1] Jour. Pharm. and Exp. Therap., 1915, 7, 295.

Mandelin's or Erdmann's reagents be added, instead of sulphuric acid itself, the same results are obtained as with the acid alone.

2. *Concentrated Hydrochloric Acid Test.*—Strong hydrochloric acid dissolves a residue containing the alkaloids of veratrum without change of color, but, on boiling this solution, a bright-red color is developed, the color persisting for days. This test is quite characteristic, although it is not very delicate, as it requires about 0.1 mg. of the mixed alkaloids for reliable results.

3. *Weppen's Test.*—Thoroughly mix 1 part of the suspected residue with 6 parts of finely powdered cane-sugar, and add a few drops of concentrated sulphuric acid, when a yellow color will appear, which changes to grass green and then to blue, the mixture finally becoming colorless. This test is quite characteristic.

Laves modifies this test as follows: To 1 cc. of pure concentrated sulphuric acid in a test-tube add 3 or 4 drops of a 1 per cent. aqueous solution of furfurol and mix. Add 3 to 5 drops of this solution to the residue, in such a way that the two materials just touch. If veratrum alkaloids are present, a dark streak will gradually run from the residue into the liquid. At the starting-point it will appear blue or blue-violet, and, farther away, green. If the residue and liquid be stirred with a glass rod, the liquid will become dark green, and, after some time, blue, and finally violet.

Biologic Test.—If a small quantity of a very slightly acid (acetic) solution of the suspected residue be injected into the lymph-sac of a frog, there occur movements as if the animal were about to vomit, the heart's action is immediately slowed, and a curious clumsiness and awkwardness in the movements becomes apparent, which shortly indicate spasmodic contractions of the muscles and an inability to relax them. If the dose be sufficiently large, tetanic spasms and symptoms of paralysis predominate from the start.

CHAPTER XXII

NON-ALKALOIDAL ORGANIC POISONS

In this chapter we shall discuss a somewhat heterogeneous group of compounds, embracing hydrocarbons of both the aliphatic and aromatic series, with many of their derivatives, some of the heterocyclic compounds, oils of various types, glucosides, and a few miscellaneous vegetable principles, which are difficult to classify under any special heading. There is no attempt to include all remaining poisons, but, rather, to consider only those associated with the more usual cases of poisoning.

PARAFFIN HYDROCARBONS

The constituents of American petroleum having low boiling points, consist almost entirely of saturated hydrocarbons, although very small quantities of some of the benzene (aromatic) hydrocarbons are present, The gas coming from oil or gas wells consists chiefly of hydrogen, methane, and ethane, while the liquid pumped from the wells still holds ethane, propane, and butane in solution, which gases may be removed by distillation. The somewhat higher fraction contains largely butane and pentane, and is, often, used as fuel for gas stoves. By fractional distillation of the crude oil, left after these more volatile gases are removed, several products of industrial and commercial value are obtained; Petroleum ether, consisting chiefly of pentane and hexane, and boiling between 40° and 70°C.; gasoline, composed mostly of hexane and heptane, and boiling between 70° and 90°C.; naphtha, made up of heptane and octane, and boiling between 90° and 120°C.; benzine, consisting of octane and nonane, and boiling between 120° and 150°C.; and kerosene, containing the higher hydrocarbons from decane to hexadecane, and boiling from 150° to 300°C. The members of this series above hexadecane are solids at body temperature and exert practically no toxicologic effect.

These mixtures of the low boiling point hydrocarbons are poisonous when inhaled in the form of vapor, or when taken in the liquid form by mouth. The poisoning by inhalation is, ordinarily, industrial or accidental, and has occurred, rather frequently, in those engaged in cleaning tank cars or storage tanks, which had contained these products; among those engaged in the care and repair of automobiles; in industries, such as the rubber industry, in which these agents are used as solvents; among painters using paints containing these volatile hydrocarbons as substitutes for turpentine; and in "dry cleaning", in which process these substances are used to remove grease from clothing. Friedberger[1] reports the poisoning of a child from whom plasters were removed with benzine; while Houghton[2] records the poisoning of a woman from washing her hair with gasoline in a small bathroom. Occasionally these products have been taken with suicidal intent.

These volatile products belong to the class of anesthetics, but differ from the usual ones in that they have practically no serious after effects. Applied locally they are irritants of mucous membranes, and, in contact with the skin, produce a dermatitis, many cases of which are seen arising from wearing of gloves recently cleaned with gasoline or benzine, or from the saturation of clothing with gasoline while cleaning engines, or from application to the hands in cleaning type, metal, etc. After absorption their effects are somewhat similar to those of the alcohol-ether group of anesthetics, although their anesthetic action is weak from a practical point.

Symptoms.—Administered to man by inhalation, these hydrocarbons cause dizziness, nausea, vomiting, a burning sensation in the chest, drowsiness, and sleep. In cases of slight poisoning, the symptoms resemble those of mild alcoholic intoxication, constituting the so-called "naphtha jag", lack of self-control being a prominent symptom, and muscular irritability being more or less marked during the stage of excitement. These effects are followed by depression, headache, nausea, roaring in the ears, irritation in the throat, trembling in the hands and arms. In the more severe cases, signs of respiratory failure appear, the patients become pale, the lips livid, respiration slow, heart weak and feeble, followed by insensibility, convulsions, and death from respiratory failure. Schustrow and Salistowskaja[3], in their experimental work on rabbits and guinea-pigs, found an aplastic hemolytic anemia, increased fragility of the red cells, and a leukopenia affecting all white cells, the serum containing less cholesterol than that of the control animals. These workers found, also, an increasing resistance or habituation to benzine, following repeated doses, and attribute this to the loss of fat in the poisoned animals and, consequently, to the diminished absorption by the blood.

If the low boiling hydrocarbons be ingested, the symptoms consist of dyspnea, cyanosis, unconsciousness, coldness of the skin, and dilatation of the pupils. With *kerosene*, poisoning from which is not uncommon, the symptoms are, at first, referable to the irritation of the gastro-intestinal tract. There are a burning pain in the throat and stomach, vomiting, colicky pains, diarrhea, thirst, etc., followed by cyanosis, labored respiration, and unconsciousness, death being rare. Barbour[4], who reports 4 cases of kerosene poisoning, one of which was fatal, calls

[1] Münch. med. Wchnschr., 1912, **59**, 252.

[2] Brit. Med. Jour., 1908, **2**, 1747.

[3] Deutsches Arch. f. klin. Med., 1926, **150**, 271 and 277.

[4] Jour. Amer. Med. Assoc., 1926, **87**, 488.

attention to the bright cherry-red color of the lips. In one of his cases, the red blood cells were not appreciably affected, but there was a distinct leukocytosis, the blood spectrum showing methemoglobin.

In cases of chronic poisoning, some of which have been reported, the symptoms were abdominal pain, nausea, vomiting, weakness and heaviness of the arms and legs, paresthesias, dizziness, and drowsiness, and, occasionally, a chronic mental state simulating feeblemindedness. Workers in the petroleum and paraffin industries, and in associated trades, not infrequently show a variety of skin lesions, partly due to the irritant action of the products, and in part to infection(oil folliculitis).

Fatal Dose.—This is a difficult matter to state. Inhalation requires less to produce dangerous symptoms than does ingestion. According to the Bureau of Mines[1], 11,000 to 22,000 parts of gasoline vapor per million of air is a dangerous concentration for even short exposure, while 24,300 parts per million are rapidly fatal for short exposure. It is probable that there is only a narrow margin between the concentration which produces anesthesia and that which causes death. When ingested, 10 to 15 grams (1/3 to 1/2 ounce) of benzine have proven fatal in from 10 minutes to 4 hours; 30 grams (1 ounce) has caused death in 5 hours; while 250 cc. and more have been recovered from.

Treatment.—If the poisoning is by inhalation, the patient should be removed as quickly as possible from the contaminated atmosphere, and the clothing of the patient should be changed if it has been in contact with the liquid. Warm baths should be given, and artificial respiration resorted to, if respiratory failure is threatened. If the hydrocarbon has been ingested, the stomach should be washed out with copious quantities of warm water. The after-treatment is purely symptomatic.

Postmortem Appearances.—There is nothing characteristic in the autopsy findings, beyond the possible odor of the hydrocarbons in the stomach contents or in the lungs. If ingested, these products produce hyperemia and small hemorrhages in the gastro-intestinal tract, occasionally hemorrhages in the lungs, and slight hemolysis. The blood may show the presence of methemoglobin.

Detection.—The stomach and contents should be especially examined if the poison be ingested, while the lungs and brain may afford the best results if death is due to inhalation. The tissues should be finely ground and submitted to fractional distillation starting the process at a low temperature and increasing it gradually, in order to isolate, if possible, the products of different boiling points. The distillates should then be examined with reference to their odor, boiling points, and other physical properties.

HALOGEN DERIVATIVES

"The halogen compounds of the aliphatic hydrocarbons", state Henderson and Haggard[2], "are more active pharmacologically than the hydrocarbons from which they are derived. This increased activity is not due to any action of the halogen on the tissues, but to the entire molecule of the substance. The chlorine derivatives are decomposed in the body to only a small extent; the iodine and bromine compounds with the methyl and ethyl groups are, however, more or less rapidly hydrolyzed into the corresponding alcohol or other hydrocarbon, and hydriodic and hydrobromic acid."

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[1] Technical Paper No. 272, 1921.

[2] *Noxious Gases*, 1927, p. 158.

Methyl Chloride

This halogen compound (CH_3Cl) is a colorless, non-corrosive gas of a peculiar, sweetish odor, and has a specific gravity of 0.920 at 18°C. At lower temperatures it condenses to a liquid which boils at -23.7°C. It is soluble in both water and alcohol, 1 volume of water dissolving 4 volumes of methyl chloride, while 1 volume of alcohol dissolves 35 volumes of this compound. It is used in various chemical processes as a methylating agent, and is finding rather wide application as a refrigerant.

Poisonings from this compound are practically all due to inhalation of the gas in plants engaged in the manufacture of refrigerating machines in which this gas is employed, or from sudden or undetected leaks in multiple systems installed for domestic purposes. It is probable that the intake of aqueous or alcoholic solutions or of lipoid foods or liquids, which have been exposed to the gas from a leak in the refrigerator, plays only a minor part in such poisonings, although a mild narcotic effect of the alcoholic solution was observed in the investigations of a committee on anesthetics of the British Medical Association[1].

Although Eulenberg in 1876 reported the toxic action of methyl chloride on pigeons and Kionka in 1900 discussed the comparative toxicity of this compound, the first reports of accidental poisoning were made by Gerbis[2] in 1914, who studied the cases of two mechanics affected by the gas while repairing a leak in an ice machine, both workmen recovering after about 2 weeks. Roth[3] reports two further non-fatal cases and discusses 8 other cases, which were later presented in detail by Schwarz.[4] Of the 10 cases of Schwarz, one was fatal, this latter being mentioned by Zangger[5]. In 1927 Baker[6] reported 21 cases with no deaths among the employees in a factory manufacturing refrigerating machines. Kegel, McNally and Pope[7] state, "Since August, 1928, there have been reported in Chicago twenty-nine cases of poisoning by commercial methyl chloride gas, with ten deaths. All of these cases, except three, which occurred in a plant where methyl chloride refrigerators are manufactured, developed in kitchenette apartments where leaks were discovered in the refrigerating system." While it is probable from the history of these cases that they were, in reality, due to methyl chloride poisoning, yet only 7 of these were *proven* to be such. These 7 cases were examined by the writer and Jaffé and definitely established as due to methyl chloride poisoning by the symptoms, pathological, and chemical findings in the organs of the dead individuals. As a further check on the possibility of fatal poisoning from this gas, guinea-pigs were exposed to the gas in the kitchenette apartments in which the human deaths had occurred, and the animals were found dead after an exposure of several hours. Chemical and pathological examination of these organs confirmed the cause of death.

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[1] Brit. Med. Jour., 1879, **1**, 1.

[2] Münch. med. Wchnschr., 1914, **61**, 879.

[3] Schweiz. Ztschr. f. Unfallkunde, 1923, **17**, 169.

[4] Deutsch. Ztschr. f. d. g. ger. Med., 1926, **7**, 278.

[5] "Die organischen Gifte" in *Lehrbuch der Toxikologie* by Flury and Zangger, 1928, p. 203.

[6] Jour. Amer. Med. Assoc., 1927, **88**, 1137.

[7] Ibid., 1929, **93**, 353.

While it has been a belief among manufacturers of methyl chloride refrigerators that this gas is incapable of producing fatal results, yet Schwarz has reported 1 fatal case and many serious poisonings have occurred among the workmen in the plants. In this connection it is to be mentioned that the conditions under which these workmen inhale the gas are different from those existing in the apartment in which a multiple-unit methyl chloride refrigerator is installed. The workmen are instructed to leave the point of exposure and seek fresh air just as soon as they notice any signs of headache or dizziness, so that immediate effects soon wear off. With the occupant of the apartment, however, such symptoms lead the exposed individual to lie down, and, under these circumstances, more of the gas is inhaled, so that the insidious action of the gas increases until the individual becomes drowsy and soon unconscious, from which state he may never recover. If the leak occurs during the night, the sleeping individual may be aroused by the desire to vomit, but he may be so weak that he can not arise, and so remains in his bed until overcome, as was the case with 3 of the individuals, whose organs were examined by the writer. It is very probable that more such cases will occur in the future, unless some provision is made for mixing with the practically odorless, nonirritating methyl chloride a warning gas that has such distinctly irritating qualities that the exposed individual must seek fresh air at once.

Symptoms.—The symptoms noted after inhalation of methyl chloride vary with the concentration of the vapor and the time of exposure. Short exposure to the gas causes headache, dizziness, weariness, and a desire to sleep, all of which symptoms may disappear if contact with the gas is discontinued. Longer exposure, or short exposure to high concentrations, causes marked vertigo, apathy, anorexia, pains in the abdomen, vomiting and diarrhea, disturbances of vision, staggering gait, with a feeling of buoyancy described by Baker as a sensation of "walking on air" (the general condition being known in the refrigerating trade as a "methyl jag"). Later, there may be weakness in the legs, cyanosis, convulsive and labored breathing, and profound coma, which may last for several days. Before death clonic and, in some cases, tonic convulsions may occur.[1] The early symptoms may closely resemble those of intoxication with alcohol. If the patient recovers, there may be mental disturbances of various types, which may last for some time. In many of the cases observed the breath had a peculiar, sweetish odor. The urine may be acid or alkaline and contains formic acid in proportion to the severity of the poisoning, while acetone has been found in some of the cases. The blood picture is suggestive of a primary anemia, and an eosinophilia may be noted. In 16 out of the 21 cases reported by Baker visual disturbances were noted, varying from slight blurring to diplopia, which might suggest the action of the methyl alcohol liberated in the system. In 4 of the fatal cases seen by the writer, the patients were in coma for periods varying from 12 to 36 hours, while in the other 3 cases, death occurred more rapidly, although the exact time elapsing between exposure and death was not known.

Fatal Dose.—As this compound is decomposed to some extent in the system, although more slowly than are methyl bromide and methyl iodide, methyl chloride does not tend to accumulate in the system, but the methyl alcohol does, so that the poisoning may, in reality, simulate one with methyl alcohol. As Henderson and Haggard[2] state, "The marked accumulative property of methanol and its destructive action upon the nervous system render these three methyl halides particularly poisonous. They do not themselves accumulate in the body and reach an equilibrium preventing further absorption, as in the case of non-reactive gases, but are decomposed with the production of methanol. Consequently methanol continues to accumulate in the body as long as the exposure persists. Thus severe poisoning by methanol results after prolonged exposure to concentrations of a methyl monohalide too small to exhibit the anesthetic action of the undecomposed substance." A contributing factor in the poisoning is the acidosis due to the presence of the hydrochloric acid arising from the decomposition of the methyl chloride.

The lethal concentration of methyl chloride for man has not been definitely determined. As compared with chloroform, methyl chloride is about ¼ as toxic according to Kionka[3]. It is probable that a concentration of 0.4 per cent. of methyl chloride in the air of an apartment would prove fatal, if inhaled for several hours. For animals the lethal concentration has been investigated by the Bureau of mines[4]. A vapor concentration of 41.5 per cent. methyl chloride in air by volume caused rapid loss of equilibrium, and the animals were unable to stand after 30 seconds. This condition was followed by a rapid, convulsive, and gasping type of respiration and death in 8 minutes. Practically the same symptoms occurred in animals exposed to 15.3, 14.7, and 11.9 per cent. vapors, although death did not occur until a day or more following an exposure of 10 to 20 minutes. Exposure to 9.5 per cent. vapors caused dizziness in 2 minutes and inability to walk in 10 minutes. All animals exposed for 10 to 110 minutes to concentrations of 9.5 to 15.3 per cent. died in 1 to 4 days later. Exposure to lower concentrations proved fatal in proportion to the time of exposure. Thus, concentrations as low as 0.50 to 0.56 per cent. methyl chloride caused no marked symptoms except an increased rate of respiration after 540 minutes, though death occurred in all animals in 1 to 2 days following 120 and 270 minute exposure periods, and in 2½ to 15 hours following 540 minutes exposure; while animals exposed to 0.12 to 0.15 per cent. vapors died 2 to 3 days after periods of exposure ranging from 270 to 810 minutes. It is clear, therefore, that poisoning with methyl chloride is of an insidious nature, as exposure to the low concentrations, which may exist as a result of a slight leak in a refrigerating system, may cause only slight preliminary symptoms, which may be disregarded by the victim, but will be followed after prolonged exposure by severe symptoms with coma and death in a few days.

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[1] See *Lehrbuch der Toxikologie* by Flury and Zangger, 1928, p. 203.

[2] *Noxious Gases*, 1927, p, 159.

[3] Arch. internat. de Pharm., 1900, 7, 475.

[4] "Physiological Response Attending Exposure to Vapors of Methyl Bromide, Methyl Chloride, Ethyl Bromide and Ethyl Chloride" by Sayers, Yant, Thomas, and Berger, Public Health Bulletin No. 185, March, 1929.

Treatment.—This should consist in immediate removal of the subject from contact with the gas. In some cases consciousness may be regained after a variable period, while in others the coma passes into death. Alkalies are indicated by mouth (if the subject can swallow), or by rectum, while glucose subcutaneously or per rectum in the form of a 5 per cent. aqueous solution may prove valuable. Inhalation of oxygen should be begun early and continued until the peculiar odor of the breath has disappeared. In some cases artificial respiration may be necessary, until the patient begins to breathe naturally. If convulsions occur, these may be controlled by bromides. The later treatment is symptomatic.

Postmortem Appearances.—All the changes noted vary from slight to marked, depending largely on the concentration of the vapor and the period that elapsed before death. The lungs are markedly hyperemic and, sometimes, edematous. The heart may be dilated and filled with dark, fluid blood, and petechial hemorrhages are found in the epicardium and endocardium. The liver is hyperemic and shows evidence of fatty degeneration. The kidneys, brain, and spleen are markedly hyperemic. The suprarenals are, in some cases, congested and edematous. The changes in the stomach and intestines appear to be limited to a slight hyperemia. These changes have been shown in the fatal human cases and in the organs of the experimental animals.

Detection.—It is possible that little may be expected in the way of chemical detection of methyl chloride, per se, in the tissues, although, if death be rapid from exposure to high concentrations, some will, undoubtedly, be found in the blood and fresh tissues, as was the case in two of the subjects examined by the writer. The detection of methyl chloride may be carried out in two ways: (1) The blood and finely ground tissues are rubbed up with strong alcohol, and placed in a flask. Pass hydrogen through the apparatus, and, after the oxygen is expelled, light the evolved gas. On placing a copper gauze in the hydrogen flame, a bluish-green color will be developed in the presence of methyl chloride; (2) Place some of the blood in a small flask and distill slowly, passing the vapors over heated platinum foil, when hydrochloric acid and carbon dioxide will be formed.

Formic acid is found in the urine, if the tests are made early, and, in some cases, even before symptoms develop, so that the urine should always be examined in suspected cases. The chief reliance, especially in the protracted cases, must be laid upon the detection of methyl alcohol, formaldehyde, and formic acid in the tissues, but, often, these may not be found. These examinations may be accomplished by examining the distillate from acid solutions, the tests outlined under methyl alcohol and formaldehyde being employed.

Should one wish to test the air in the apartment for methyl chloride, a simple method is as follows: Heat a piece of copper gauze or wire in the nonluminous gas flame. If a volatile halide be present, the flame is colored an intense greenish-blue. Such a test might well be employed by the householder in determining for himself whether or not the air in his apartment is contaminated. Quantitative determination of the concentration in the air may be accomplished by passing a measured amount of air over heated platinum foil, collecting the hydrochloric acid which is formed by the decomposition, and determining the amount of acid. A simple calculation yields the amount of methyl chloride equivalent to the hydrochloric acid found.

METHYL BROMIDE

Methyl bromide (CH_3Br) is, at ordinary temperatures a gas of a marked ether-like odor, the boiling point of the liquid form being 4.5°C. It finds no use in medicine, but is employed extensively in chemical industries, especially in the manufacture of dyes and of such compounds as antipyrine. Accidental poisonings have arisen through defects in apparatus, leaks in distillation tubes, etc.[1]

Symptoms.—As early symptoms one may observe headache, weakness, vertigo, vomiting, and some disturbance of vision. The gait may be staggering, while slight pain in the extremities, neuritic symptoms, and visual disturbances may be noted. After an interval of hours or even days, during which the subject may feel fairly comfortable, severe symptoms appear in the form of strong contractions of different groups of muscles, clonic spasms of the entire body, double vision, pareses of the extremities, sleepiness, and polyneuritis. Convulsive type of respiration may be noted, and, in the fatal cases reported, epileptiform attacks are merged into a terminal coma. Physical signs of pneumonia may be observed. Convalescence is slow, in some cases being a matter of weeks, while in others after months or even years disturbances of coordination, uncertain gait, increased reflexes, weariness, and failing memory have been observed.

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[1] See Goldschmid and Kuhn, Zentralbl. f. Gewerbehyg., 1920, **8**, 28; Rohrer, Vrtljschr. f. ger. Med., 1920, **60**, 51; Loeffler and Rütimyer, Ibid., 60; Cade and Mazel, Bull. Soc. méd. des Hôp. de Paris, 1923, **47**, 722.

Methyl bromide is decomposed relatively soon in the system, the toxic symptoms being related to the formation and action of methyl alcohol and hydrobromic acid. The toxicity of methyl bromide is greater than that of methyl chloride, due, possibly, to the increased decomposition of the former. Atmospheres containing 5 and 9.6 per cent. by volume of methyl bromide cause immediate uneasiness to animals and death in 7 to 15 minutes[1]. Concentrations of 2.2 per cent. induce coughing in 7 minutes, followed by a retching-like action and unsteadiness in 8 to 15 minutes, and marked weakness in 30 minutes. Vapor-air mixtures containing 1.3 per cent. methyl bromide caused increased respiration in 13 minutes; inactivity, lachrymation, discharge from the nose, weakness and unsteadiness in 23 to 28 minutes; convulsive respiration and death in 43 to 68 minutes.

The pathological changes observed are practically the same as those discussed under methyl chloride. The degree of these changes varies with exposure, but in general "the changes were most severe in animals that died immediately after or within 24 hours following long exposure to comparatively low concentrations."

ETHYL CHLORIDE

Ethyl chloride (C_2H_5Cl) is official, and appears, at low temperatures or under pressure, as a colorless, mobile, liquid with a characteristic ethereal odor and a burning taste. Its specific gravity at 0°C. is about 0.921, while its boiling point is between 12° and 13°C. This liquid is very volatile, and burns with a smoky, greenish flame with the production of HCl. It is slightly soluble in water, and freely soluble in alcohol and in ether.

It is used as a local anesthetic, and has been used as a general anesthetic for minor operations of short duration. Not infrequently it leads to poisoning, some of them fatal, Glaister[2] stating that "From twenty to thirty deaths while under its influence have been recorded in this country."

This halogen compound is decomposed in the system into ethyl alcohol and hydrochloric acid. As the ethyl alcohol is oxidized rapidly into carbon dioxide and water, there is little action of the decomposition products, so that any toxic action must be exerted before the compound decomposes, which action is different from that of the methyl compounds, as there is no accumulation of the alcohol with the ethyl derivatives.

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[1] See Sayers, Yant, Thomas, and Berger, Pub. Health Bulletin No. 185, March, 1929.

[2] *Medical Jurisprudence and Toxicology*, 4th ed., 1921, p. 759.

Symptoms.—Inhalation of this compound produces the symptoms of anesthesia, much as do chloroform and ether, although not quite so markedly. It acts as a stimulant of the vaso-motor system, but produces paralysis of the myocardial muscles, disturbs its conductivity, and is very liable to induce cardiac fibrillation. The pulse is generally slowed, while the respiration is deep. Nicloux found about 20 mgs. of ethyl chloride per 100 cc. in the blood in light anesthesia, from 30 to 150 mgs. in deep anesthesia, and 40 to 180 at death. Anesthesia is obtained in about 2 to 5 minutes, although complete muscular relaxation may be absent. Recovery follows a few minutes after removal of the mask.[1]

ETHYL BROMIDE

Ethyl bromide (C_2H_5Br) is a heavy, colorless, volatile liquid, with a chloroform-like odor. It boils at 39°C. It readily undergoes decomposition on standing, the color changing to yellow. It is used in chemical industry and has been quite frequently used as an anesthetic for short operations, especially in dentistry. It is not to be regarded as an especially safe anesthetic, so that its use has been almost discontinued. According to Hunt,[2] ten volumes per cent are necessary to anesthetize animals within 5 minutes, and if this concentration is maintained for fifteen minutes, death occurs. While deaths from its use are not numerous, yet some occur. Thus in a series of 60,000 cases there were 16 deaths. Death may occur as early as 30 seconds after beginning the inhalation, or be delayed for hours or days.

Although anesthesia is produced rapidly after inhalation of ethyl bromide, yet many individuals are quite refractory to its use, being stimulated rather than depressed. It produces the same marked effects on the heart as do ethyl chloride and chloroform, and patients complain of considerable depression and discomfort after its use.

High concentrations of ethyl bromide are markedly irritant to the lungs when breathed for a short time, producing an acute congestion and edema. Low concentrations of ethyl bromide vapor (2.4, 1.2, 0.65, and 0.32 per cent) act as a toxin to the kidney, producing a diffuse acute parenchymatous nephritis, while the irritating effects on the lungs will be manifest if the exposure is continued sufficiently long to those low concentrations.[3]

CHLOROFORM

Chloroform was introduced by Simpson in 1847 as a substitute for ether in producing general anesthesia, and was widely used for this purpose until it was found to be more dangerous, so that, of late years, it has fallen somewhat into disrepute.

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[1] See Cushny's *Pharmacology and Therapeutics*, 9th ed. revised by Edmunds and Gunn, 1928, p. 236.

[2] "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2,** 670.

[3] See Waite and Yant, Pub. Health Rep., 1928, **43,** 2276.

Poisoning by chloroform has resulted, largely, from its use by inhalation, although many cases have occurred from ingestion by mouth. It is to be said, however, that the number of cases of actual poisoning is relatively small in comparison with the large number in which this drug has been used as an anesthetic. Statistics as to the number of actual fatal poisonings vary widely, but probably 1 in 3500 may be regarded as an average of the cases. Although rarely used for the purpose of *homicide*, chloroform has been credited with causing homicidal death in quite a few cases, but in all of these the anesthetic appears to have been administered by force. While there is much discussion in the literature as to the possibility of chloroforming a person while asleep[1], there are found in the literature several reliably reported cases in which sleeping adults have been completely anesthetized without being awakened, although, as a rule, the person awakes before anesthesia really begins. It is probable, however, that no authentic case is on record in which chloroform has been successfully used on a sleeping person for criminal purposes. Cases of *suicide* by inhalation of chloroform are rare, although some of this type have been reported. As Witthaus says: "There is, however, a rather numerous class of cases in which persons in the habit of self-administration of chloroform by inhalation either to allay pain, to induce sleep, or for mere enjoyment of the sensation produced, have been found dead under circumstances which have left the question of their intent an open one."

Poisoning by ingestion of chloroform has been quite frequently reported. Witthaus collates 109 such cases, of which 36 were fatal and 73 not; 56 were suicides, 36 accidents, 1 homicidal, 1 an attempted abortion, and 15 of unknown origin. According to Hunt[2] 8 fatal cases occurred in St. Louis in 1910 to 1914. This drug is not infrequently used as an intoxicant, Hofmann-Haberda[3] reporting the poisoning of a number of Russian prisoners during the war by drinking chloroform in mistake for alcohol.

Properties.—Chloroform (trichlormethane, $CHCl_3$) is a clear, colorless, mobile liquid, having a characteristic, ethereal odor, and a burning taste. It is neutral in reaction, has a specific gravity varying between 1,474 and 1,478 at 25°C., and a boiling point of about 61°C., although it is volatile at lower temperatures. It is soluble in 210 volumes of water, and is miscible with alcohol, ether, benzene, petroleum benzin, and with fixed or volatile oils. Chloroform and its vapors are not inflammable, but when heated, its vapors burn with a green flame. If used for some time near a flame, or even under the direct action of sunlight, chloroform may be decomposed into phosgene[4] (carbonyl chloride), chlorine, and hydrochloric acid, which products may lead to fatal poisoning.[1] The official preparations of chloroform are *aqua chloroformi*, *linimentum chloroformi*, and *spiritus chloroformi*.

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[1] See Witthaus, *Toxicology*, 1911, p. 1146 et seq.

[2] "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 640.

[3] *Lehrbuch der gerichtlichen Medizin*, 11te. Aufl., 1927, p. 903.

[4] See page 594.

Symptoms.—With chloroform poisoning, as with that following toxic doses of alcohol and ether, there are stages of lessened consciousness, excitement, and total unconsciousness. There is a progressive paralysis of the central nervous system, commencing with the highest cerebral centers, passing downward, then affecting the spinal cord, and last of all the medullary centers, the sensory functions being involved before the motor.

The first effects (the *first stage*) noted are a sense of suffocation, of warmth of the face and, later, of the whole body, associated with a tingling sensation of the skin. The senses become less acute, the patient seeing things vaguely and hearing things as though they came from a distance. There are ringing, roaring, and hissing sounds in the ears, and a sense of inability to move the legs and arms appears. The face is generally flushed, the pupils are slightly dilated, respiration may be irregular or quickened, while the pulse is somewhat rapid. Following these signs, a period of excitation may appear, although it is often absent. "It is characterized by tremblings, or even spasms, violent struggling, laughing, singing, inarticulate jabberings, crying, praying, or indulgence in abuse and profanity." The skin is flushed and often cyanotic, the respiration is irregular, pupils are still somewhat dilated, and pulse is rapid.

The *second stage* is that of depression or surgical anesthesia. The face assumes a death-like appearance, the muscles are relaxed, the reflexes disappear, sensibility to pain is gone, the pupils contract somewhat and may not react to light, the pulse is generally slightly slower and weaker, and the respiration is regular, but slow and shallow. This stage of anesthesia may be continued for some time by repeated inhalation of small quantities of chloroform, special precaution being taken to regulate the proportion of vapors in the air inhaled, so that approximately not more than 1.5 to 2 per cent. of chloroform vapor is present in the anesthetic mixture. If the inhalation be discontinued at this point, the patient is restored to consciousness within 20 to 40 minutes, as a rule, although he may not awake for a much longer period. If the anesthetic be pushed beyond this point, the concentration of chloroform in the blood becomes sufficient to produce serious results.

The *third stage* is that of paralysis, characterized by respiratory and cardiac failure, and by a fall in blood pressure. The surface of the body becomes cyanosed and bathed in a cold perspiration, the lips are blue, the pupils dilate widely (a danger signal in the stage of anesthesia), the respiration becomes slower and quite stertorous, and the pulse progressively slower, weaker, and irregular. Vomiting may set in at any stage of the anesthesia, but it appears to be more frequent in the later stages, and is, especially, noted after restoration to consciousness.

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[1] See Scheicher, Vrtljschr. f. ger. Med., 1920, **60**, 175; Leblanc and Binet, Arch. de Mèd. exp., 1920, **28**, 628; Laqueur and Magnus, Ztschr. f. exp. Med., 1921, **13**, 31 and 200.

Death from chloroform may result from cardiac paralysis, from stimulation of the cardio-inhibitory center, or from paralysis of the respiratory center. It seems probable that, when death occurs late in the anesthesia, the respiration ceases first. In some cases in the early stages of anesthesia, or when the inhalation is irregular or has been suspended and then resumed, the heart may suddenly become irregular, the blood pressure may fall almost to zero, and death rapidly follow, Embley[1] attributing this form of death from syncope to overactivity of the vagus nerve, while Levy[2] believes it to be due to ventricular fibrillation during *light* anesthesia, and likely to occur from sensory nerve stimulation, the excitatory effect on the heart, possibly, being reinforced by reflexes through the accelerator apparatus or by an increased secretion of the suprarenal glands.

When chloroform is swallowed, the first effects are referable to its local irritating action. As a result of this, there may be pain in the throat and abdomen, vomiting may occur, and, occasionally, purging. After absorption of the chloroform, the symptoms are much like those noted after inhalation. With small doses the period of excitement, often, resembles that noted from alcohol, while after large doses the period of depression comes on rapidly. Death may occur in coma, but in many cases it is due to gastritis, while pulmonary edema or cardiac failure may be the cause of the fatal outcome.

Delayed chloroform poisoning is a type of poisoning, which comes on after apparent recovery from the anesthetic, appearing, in some cases, 10 to 12 hours after the return to consciousness, or, more usually, developing within 24 to 48 hours, and, occasionally, being delayed for several days. The chief effects noted are due to a toxemia affecting the liver, heart, and kidneys. Following a period of restlessness, the patient vomits frequently, jaundice and tenderness over the liver develop, and the patient may pass into a deep coma, the general symptoms closely simulating those noted in phosphorus poisoning or acute yellow atrophy.[3]

Fatal Dose.—The danger of chloroform depends more upon the concentration of the vapor in the lungs than upon the actual amount of chloroform inhaled. As Cushny remarks: "The degree of narcosis and of danger is not indicated by the actual amount of the anesthetic which has been used, but by the concentration of the vapors which have been inhaled; one patient may, in the course of a long operation, inhale and again exhale many ounces of chloroform without danger, while another may be thrown into a position of extreme peril by the inhalation of a few drops of chloroform in concentrated vapor." Cases have been reported in which 30, and even 15 drops of chloroform have caused death; on the other hand, 22½ ounces have been inhaled in 24 and even in 12 housr and the patient recovered.[1] According to Kobert[2] a concentration of 200 parts of chloroform vapor per million of air (0.02 per cent.) produces only slight symptoms after several hours exposure, 5,000 to 6,000 parts per million of air (0.5–0.6 per cent.) is the maximum concentration that can be inhaled for 1 hour without serious disturbance, and 14,000 part per million of air (1.4 per cent.) are dangerous after 30 minutes to 1 hour exposure; while Lehmann[3] and Herrmann[4] show that 25,000 parts per million (2.5 per cent.) are rapidly fatal for short exposure. Henderson and Haggard[5] state: "The concentrations of chloroform in the blood causing anesthesia are between 0.2 and 1.5 grams per liter, and those causing death between 0.4 and 1.8 grams."

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[1] Brit. Med. Jour., 1902, **1,** 817, 885, 951, and 975.

[2] Heart, 1913, **4,** 319, 1914, **5,** 299; Proc. Roy. Soc. Med., 1914, **7,** Sect. on Anesth., 57.

[3] See Favill and Bevan, Jour. Amer. Med. Assoc., 1905, **45,** 691; also, Stander, Bull. Johns Hopk. Hosp., 1924, **35,** 46.

The fatal dose of chloroform, when taken by mouth, varies widely. "In ten of 96 cases", says Witthaus, "in which the amount taken is stated the subjects recovered after having swallowed one fluid ounce (44 gm.) of chloroform, while in 10 cases death followed the ingestion of that or a lesser quantity." A child of 4 years died from the effects of 1 fluidram, while adults have been fatally poisoned by doses of 15, 33, and 40 grams, and others have recovered after doses of 70, 133, 177 and 222 grams.

Fatal Period.—Death may occur during any of the stages of anesthesia. In many of the reported cases it has taken place almost before anesthesia is complete. Embley[6] states that, of 83 cases of death in England during 1899, 68 happened before the operation was started, and in another year the record was 39 out of 41. Lyman[7], in his table of 52 fatalities, tabulates 4 cases in which death occurred in less than 1 minute, 18 in from 1 to 5 minutes, 22 in from 5 to 10 minutes, 7 in from 10 to 20 minutes, and 1 in 25 minutes. When chloroform is swallowed, death has occurred in 10 minutes, and has been prolonged for 8 days. "Of 24 such cases in which the time of death is reported 7 died in 6 hours or less, 5 in from 6 to 24 hours, 6 from 24 to 36 hours, 3 in from 36 to 48 hours, and 3 in periods longer than 48 hours." In cases of delayed poisoning, death occurs, as a rule, in 4 or 5 days.[8]

Treatment.—If the respiration fails during the inhalation of chloroform, the administration should be stopped at once, the head of the patient should be lowered, and the feet raised, in order to combat the anemia of the brain. Artificial respiration should be promptly resorted to, the epiglottis should be raised by pressing forward the angle of the jaw or by pulling forward the tongue. Cardiac massage by intermittent pressure over the heart should be instituted. Strychnine, caffeine and atropine may be used as respiratory stimulants, and digitalis as cardiac tonics, but, as Cushny remarks: if the circulation is strong enough to cause the absorption of these drugs and carry them to the respiratory center and the heart, the patient will recover with the artificial respiration alone. While the injection of epinephrine has apparently saved life, in cases in which the heart has become very weak, yet the use of this drug would seem to be questionable, on account of its tendency to produce cardiac fibrillation, especially where syncope exists in the early stages of anesthesia. If the patient recovers from the anesthetic, the body should be kept warm with hot water bottles, owing to the fall of body temperature resulting from chloroform, and vomiting should be treated by the administration of cracked ice. The patient should be placed absolutely flat.

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[1] See Hunt, "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 644.

[2] *Kompendium der prak. Toxikologie.*, 1912, p. 45.

[3] Arch. f. Hyg., 1911, **74**, 1.

[4] Inaugural Dissert., Würzburg, 1911.

[5] *Noxious Gases*, 1927, p. 161.

[6] Brit. Med. Jour., 1902, **1**, 817, 885, 951, and 975.

[7] Cited by Witthaus, *Toxicology*, 1911, p. 1167.

[8] See Herb, Jour. Amer. Med. Assoc., 1911, **56**, 1312.

In cases of poisoning with chloroform taken by mouth, the stomach should be washed out with warm water or milk, and such demulcent drinks as olive oil may be given. The other treatment is symptomatic and is, essentially, the same as that outlined above, although the acute gastritis may require special attention. In the cases of delayed poisoning, subcutaneous or intravenous injections of saline should be employed. Administration of glucose, by mouth or by rectal injection, may be used to combat the acidosis. The rest of the treatment is purely symptomatic.

Postmortem Appearances.—The findings at autopsy are not characteristic. The organs may have the odor of chloroform, especially if the postmortem is performed soon after an acute death. If death is sudden, the blood may be fluid, but if death is prolonged, the blood will be found clotted in the heart and large vessels. If death is due to ingestion of chloroform, the mucous membrane of the throat, esophagus, and stomach may be hyperemic, and the contents of the stomach may have an odor of chloroform. In the delayed types of poisoning, jaundice and fatty degeneration[1] of the liver, heart, and kidneys may be observed.

Detection.—When chloroform is inhaled, it passes rapidly into the blood and is distributed throughout the body. Almost at once the chloroform begins to leave the blood, and is taken up especially by the central nervous system when anesthesia is rapid; while, if the anesthesia is slow, the other organs may contain as much as the brain. The organs of special value in the analysis are the brain, lungs, and liver, while, in some cases, the stomach may show appreciable amounts.

The *elimination* of chloroform is mainly through the lungs, but small amounts escape in the urine, perspiration and milk. The course of this elimination is quite rapid at first, and later becomes slower. The analysis should be started as soon as possible, as the chloroform may almost entirely escape from the body after a variable period, depending upon the degree of saturation of the tissues.

[1] See Haloff, Arch. f. exp. Path. u. Pharm., 1928, **134**, 168.

The isolation of chloroform from the tissues should be accomplished by distillation with steam, the receiver being kept cold with ice. Before starting the distillation, the reaction of the material should be taken; if neutral or only slightly acid, a trace of tartaric acid should be added; while, if alkaline, a special examination should be made for formic acid, as, otherwise, one will not be in a position to say whether the poisoning is due to chloroform or chloral, as the latter is decomposed in the presence of alkalies into sodium formate and chloroform. In any case, the reaction of the fluid to be distilled should be made acid, preferably with tartaric acid. To the distillate the following identifying tests should be applied, although it should be stated that many of them are given by chloral, bromal, bromoform, and iodoform, as well as by chloroform, but the odor of the distillate should put one on his guard.

1. *Hofmann's Phenyl-isocyanide Test.*—To a small portion of the distillate add a few drops of aniline and a few cc. of either aqueous or alcoholic sodium hydroxide solution, and heat gently. If chloroform be present, the penetrating, offensive, and irritating odor of phenyl-isocyanide (isobenzonitril, C_6H_4NC) is produced. This test will show the presence of 1 part of chloroform in 5000 parts of water. When aniline is heated with sodium hydroxide solution, in the absence of chloroform, a faintly ammoniacal odor is produced, but this should not be mistaken for the disagreeable odor of phenyl-isocyanide. This test is given, also, by chloral, bromal, bromoform, iodoform, and trichloracetic acid.

2. *Schwarz's Resorcin Test.*—Dissolve about 0.1 gram of resorcin in 2 cc. of water, add a few drops of 15 per cent. sodium hydroxide, and a little of the suspected distillate. Heat this mixture to boiling, when the fluid becomes yellowish-red and rarely, if ever, shows a yellowish-green fluorescence. This test is not distinctive, as the compounds mentioned above, also, give positive results.

3. *Lustgarten's Naphthol Test.*—Dissolve a little α- or β-naphthol in 1 or 2 cc. of 33 per cent. sodium hydroxide. Warm this solution to 50°C. and add a few drops of the suspected distillate. In the presence of chloroform, the mixture will become blue or blue-green. If this blue liquid be acidified, a brick-red precipitate is produced. This blue coloration with β-naphthol is less stable than that with the α-compound, the blue, in the former case changing to green and then to brown. Chloral and the other compounds mentioned above, also, give this test.

4. *Fujiwara's Pyridine Test.*—Mix 2 cc. of pyridine with 2 cc. of 10 per cent. sodium hydroxide solution, heat to boiling, and add a little of the suspected distillate. In the presence of chloroform, a pink or deep red color is produced. This test is very delicate, detecting 1 part of chloroform in 1 million of water, but it is not characteristic, as positive results are given by the substances mentioned above.[1]

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[1] See Ross, Jour. Biol. Chem., 1923, **58**, 641, for a slight modification of this test. Cole, Ibid., 1927, **71**, 173, has introduced a quantitative test based on this method. See, also, Yodomigawa, Bul. Hokuetsu Med. Soc., 1928, **43**, 358; Chem. Abs., 1929, **23**, 1080

5. *Ragsky's Test.*—This test is based on the decomposition by heat of chloroform into hexachlorbenzene, chlorine, and hydrochloric acid. The suspected tissue, mixed with water, is placed in a flask provided with a doubly perforated cork, through one hole of which passes a funnel tube, and through the other a delivery tube bent at right angles. The flask is placed on the water-bath and connected with a piece of hard glass tubing 18 inches long, which is heated for about 4 inches by a Bunsen burner fitted with a fish-tail burner. About 4 inches beyond the heated portion the tube passes through a Liebig's condenser about 6 inches in length, and beyond the condenser a piece of filter-paper, moistened with a mixture of starch-paste and potassium iodide, is placed in the tube. The end of the tube is connected with a receiving vessel, containing a solution of silver nitrate, and this, in turn, connected with an aspirator.

After the tube has been heated to a bright redness, the mixture in the flask is distilled at a gentle heat (60° to 70°C.), while a current of air is slowly drawn through the apparatus by the aspirator. Any chloroform vapor present is decomposed on passing through the heated tube into the products previously mentioned. The hexachlorbenzene[1] (perchlorbenzene) is deposited on the cool part of the tube in front of the flame as brilliant, needle-shaped crystals, the chlorine decomposes the potassium iodide, yielding a blue color with the starch, while the hydrochloric acid passes into the receiver and is precipitated as silver chloride. This test is very delicate and may be used almost to the exclusion of the other tests, although it is much more complicated. It may, also, be employed as a quantitative test, the precipitate of silver chloride being collected and weighed in the usual manner. The calculation is based on the following equation:

$$6CHCl_3 = C_6Cl_6 + 6HCl + 6Cl$$

Multiply the amount of silver chloride obtained by 0.25429 to obtain the equivalent of HCl, and then multiply this figure by 3.2745 to get the amount of chloroform yielding this quantity of hydrochloric acid.

Quantitative Determination.—Instead of using the above method of Ragsky or that of Ludwig, in which all of the chlorine in chloroform is converted into hydrochloric acid, this being estimated as silver chloride, the writer prefers the method of Nicloux[2] for the quantitative estimation.

Finely hash 100 grams of the suspected tissue, mix with 475 cc. of alcohol and 25 cc. of 5 per cent. alcoholic tartaric acid solution. The mixture is placed in a Kjeldahl flask fitted with a cork through which passes one tube of a Fresenius bulb, to whose other tube a continuation is fused which is bent downward and reaches to the bottom of a graduated cylinder in such a manner that its point is below the level of 10 or 15 cc. of alcohol placed therein, and 200 cc. are distilled over, all of the chloroform present in the tissues passing over in this distillate. Transfer the distillate to an Ehrlenmeyer flask, washing the cylinder with 10 cc. of alcohol. Now add to the mixture in the flask 10 cc. of a 10 per cent. alcoholic solution of sodium hydroxide (free from chlorine), and heat under a reflux condenser for an hour or more. In this process the chloroform is converted into sodium chloride and formate. After cooling, accurately neutralize the mixture with sulphuric acid, using phenolphthalein as an indicator, add 0.5 cc. of a 5 per cent. aqueous solution of neutral potassium chromate, and titrate the chlorine present with a standard solution of silver nitrate containing 8.535 grams per liter, 1 cc. of which represents 2 mg. of chlorine. If the figure obtained in this titration be multiplied by 3.367, the result is the amount of chloroform in the 100 grams of tissue taken for the test.

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[1] If the tube be heated to dull redness, monochlorethane and tetrachlorethylene may be formed, while, occasionally, carbon is deposited. In the process of Ludwig the chloroform vapor is passed through a tube heated to a high temperature, in which procedure all of the chlorine is converted into HCl. This latter process serves as a very common quantitative method for chloroform.

[2] Compt. rend. Soc. de Biol., 1906, **60**, 88. See, also, Nicloux, Ibid., 1924, **91**, 1282. for a micro-test based upon this method.

BROMOFORM

Bromoform (tribrommethane, $CHBr_3$) is no longer official. It is a heavy, oily, colorless liquid, with an odor similar to that of chloroform. It has a specific gravity of 2.9 and a boiling point of 151°C. This bromine derivative has anesthetic properties, like those of chloroform, but it cannot be used by inhalation owing to its very low volatility.

It has been used somewhat extensively in whooping-cough, in consequence of which use quite a few cases of poisoning have occurred, some of them fatal. Long continued use of the drug produces fatty degeneration of the liver and other organs, similar to that caused by chloroform in the delayed cases.

The symptoms noted after its use are much like those shown after ingestion of chloroform. While poisonous symptoms have occurred from as little as 3 drops, and about 15 drops produced severe poisoning in a child, yet neither of these cases were fatal. Death has, however, been caused by 3.75 cc. in 5 hours,[1] while recovery has followed 4, 6, and, possibly, more grams.

Detection.—Bromoform is recovered from the tissues in the same manner as is chloroform, although the temperature of distillation must be somewhat higher. The tests for bromoform are the same as those given by chloroform, the former yielding all of the tests outlined for the latter, but, with the Ragsky test, silver bromide is, of course, formed instead of silver chloride. To differentiate this bromide from the chloride, filter and dry the precipitated halide. Fuse this with a mixture of sodium and potassium carbonate, cool the fusion, thoroughly extract the residue with hot water, and filter. To the filtrate add sulphuric acid until the reaction is acid, and then add a few drops of concentrated acid, following this with chloroform. On shaking the mixture, the chloroform takes up the liberated bromine, and assumes a brown color.

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[1] Müller, Münch. med. Wchnschr., 1908, **55**, 1211.

The determination of bromoform is made in the same manner as that of chloroform, the precipitated silver bromide being weighed as such.

IODOFORM

Iodoform (triiodomethane, CHI_3) is widely employed as an application to wounds, skin diseases, and burns, and has, rarely, been used internally, especially, as an intestinal disinfectant. It may be used in the form of a dusting powder, as an ointment, or in the form of gauze saturated with it. Practically all the cases of poisoning with iodoform have arisen from the absorption from large, abraded, or ulcerated surfaces, or when large abscess cavities have been packed with the gauze. While a few cases have occurred from its internal administration, there do not appear to be recorded any instances of homicidal or suicidal death arising from its use.

Properties.—Iodoform occurs in the form of a fine lemon-yellow powder, or as lustrous hexagonal crystals, possessing a very penetrating, persistent, and disagreeable odor and taste. It is practically insoluble in water, but 1 gram is soluble in 60 cc. of alcohol, 80 cc. of glycerin, 10 cc. of chloroform, 7.5 cc. of ether, 2.8. cc. of carbon disulphide, and in 34 cc. of olive oil, at 25°C. Its solutions are neutral to litmus. It melts between 115° and 119°C., and is only slightly volatile at ordinary temperatures, but distills readily with steam.

Symptoms.—The symptoms of iodoform poisoning are somewhat varied, as part of the drug is absorbed as such and produces a marked effect upon the brain, while part is readily decomposed in the presence of alkaline fluids and in protein solutions into iodine and iodides, both of which may exert the action. Further, some of the symptoms are due to abnormal activity of the thyroid.

The symptoms generally set in with anxiety, depression, and discomfort. There may be malaise for some time, the patient becomes sleepless and restless, complains of giddiness and headache, and may, especially in the milder cases, become nauseated and vomit. The pulse is generally greatly accelerated, while the respiration does not appear to be much affected. The patient may then pass into a condition of depression, deepening into true melancholia with hallucinations and delusions of persecution. As a general rule, says Cushny, this melancholia is followed by attacks of violent delirium and mania, lasting for hours or days, and in fatal cases, by collapse and death. In other cases the patient may pass into permanent insanity and dementia. Rarely, the patient may pass into a deep sleep, and then into stupor and collapse without any symptoms of cerebral excitement.

Iodoform has no marked local action on the skin or mucous membranes, but some cases show an idiosyncrasy to its action, manifested by redness and swelling about the wound, and, occasionally, a wide-spread eruption and, even, lymphangitis. In some cases death has resulted from such action.

Hunt and Gettler[1] call attention to a chronic type of poisoning, which follows long-continued use of iodoform, the special features of this form being dyspepsia, loss of weight, eczema and other skin eruptions, palpitation of the heart, and sometimes amblyopia.

Fatal Dose.—Owing to individual susceptibility, the amount of iodoform that may cause death is uncertain. Very severe symptoms have followed the application of 11 grains to the uterus, 30 grains taken internally have caused death, while 120 grains per os have not caused a fatal outcome. Death may occur as early as 1 day, or it may be delayed for days or weeks.

Treatment.—If the poisoning has occurred from external application, prompt removal of the dressings should be carried out. The strength of the patient should be maintained, and stimulants or sedatives given, depending on whether there is cerebral depression or stimulation, potassium bromide being highly recommended as a sedative. Sodium bicarbonate may be administered by mouth, and, if the case be severe, intravenous or subcutaneous injection of normal saline should be carried out.

If the poison had been ingested, prompt gastric lavage should be practiced, along with the measures advocated above.

Postmortem Appearances.—Fatty degeneration of the heart, liver and kidneys is frequently found. Pulmonary edema, acute glomerulonephritis, and congestion of the meninges may be observed.

Detection.—The stomach-contents, kidneys, liver, brain, blood, and urine are especially suitable for analysis. Iodoform gradually decomposes in the system, the iodine being eliminated in the urine and saliva, perspiration, and bronchial secretion. Apparently the tissues hold the iodoform for some time, as iodides have been found in the urine for a month or more after the administration of iodoform.

Finely hash the organs to be examined, mix with water to a pasty consistence, render the mixture alkaline with sodium hydrate, or acid with phosphoric acid, and submit to distillation with steam. The distillate will appear milky, if iodoform is present. Render the distillate slightly alkaline with sodium hydroxide and extract the iodoform with ether in a separatory funnel. Allow the ether to evaporate spontaneously at room temperature, when the iodoform may appear in the form of yellow hexagonal stars, plates, etc. In case interfering substances are not present, the odor of the distillate may be characteristic.

To identify the residue as iodoform, apply the tests outlined under chloroform to an alcoholic solution, and, in addition, make the following test:

Lustgarten's Test.—To a little sodium phenolate[2] in a small test-tube add 2 or 3 drops of the alcoholic solution of the residue, and warm gently over a small flame. In the presence of iodoform a red precipitate forms on the bottom of the tube, which is soluble in alcohol with a carmine-red color. This red deposit is rosolic acid, and is formed by chloroform, chloral, and bromoform, as well as by iodoform.

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[1] "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 656.

[2] Prepared by dissolving 20 parts of phenol and 40 parts of sodium hydroxide in 70 parts of water.

Fusion Test.—To distinguish iodoform from chloroform and bromoform, fuse some of the residue with a mixture of sodium and potassium carbonate, cool the fusion, and extract with warm water. Filter and acidify the filtrate with sulphuric acid, and then add a few drops of concentrated acid. On shaking this mixture with chloroform, the solvent will assume a violet color in the presence of iodine derived from the iodoform.

Determination.—To the residue obtained from the distillation and extraction with ether, add some alcoholic potash and boil under a reflux condenser for an hour. Evaporate off the alcohol, dilute with water, acidify with nitric acid, precipitate the iodine as silver iodide, filter through a Gooch crucible, dry and weigh. Proper calculations will yield the amount of iodoform in the amount of tissue taken for analysis.

CARBON TETRACHLORIDE

Carbon tetrachloride finds rather wide use in industry and the arts, as a non-inflammable solvent for grease, fat, and rubber, as a constituent of certain paints, as an agent for extinguishing fires ("pyrene"), and, medicinally, as a delousing agent and an anthelmintic (especially against hook-worm infection).

Workers in trades employing carbon tetrachloride may show irritation of the eyes, nose, and throat, dermatitis, loss of appetite and weight, nausea, and headache, while, in some cases, there may be an anemia and a toxic jaundice. When heated, or exposed for long periods to light, it may decompose into phosgene[1], chlorine, and hydrochloric acid, so that there is a potential danger of poisoning from these substances. It is by no means to be regarded as a harmless drug, when taken internally, as some deaths have occurred from its administration, and its external application has lead to fatal results[2].

Properties.—Carbon tetrachloride (tetrachlormethane, CCl_4) is a clear, colorless, mobile liquid, with a characteristic odor, resembling that of chloroform. It is not inflammable, but is slowly decomposed by light, more rapidly by heat, into phosgene, chlorine and hydrochloric acid. It is soluble in 2000 times its volume of water, and is miscible with alcohol, chloroform, ether, benzene, and petroleum benzin, while it dissolves most of the fixed and volatile oils. It boils between 76° and 77°C., and has a specific gravity ranging from 1.588 to 1.590 at 25°C.

Symptoms.—This drug has much the same anesthetic action as has chloroform, producing an initial period of excitement followed by anesthesia and sleep, from which the individual may recover in a short time. It is, however, not used as an anesthetic, owing to its irritant action and its injurious action on the heart. It has a somewhat mild irritant local action, when taken internally, and eructations and a feeling of warmth in the epigastrium may be experienced, or, in some cases, nausea and vomiting. Following this local action, a latent period of 24 to 36 hours usually existing, a general action may be observed, in headache, dizziness, drowsiness, occasionally convulsions, cardiac weakness, intestinal hemorrhages, collapse, and death. In some cases, bilirubinemia and bilirubinuria may obtain, while severe attacks of pain and hematuria have been reported.

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[1] See page 594.

[2] See Veley, Lancet, 1909, 2, 1162, who reports a fatal case from its use as a dry shampoo.

Individuals differ in their resistance to the action of carbon tetrachloride. The use of alcohol, starvation and, in general, a poorly nourished condition of the person, and the administration of fatty articles of food seem to lessen the resistance and definitely increase the toxicity of the drug, while a diet rich in carbohydrates increases the resistance of the individual.[1] Calcium deficiency, or a lack of calcium reserve may explain some of the untoward results noted.[2] Absorption is largely from the intestine, while elimination occurs through the lungs and the unabsorbed portion passes out with the feces.[3]

Fatal Dose.—This is a difficult matter to state, owing to individual susceptibility. While the Pharmacopoeia gives, as the average dose, 2.5 cc. as an anthelmintic, death of an adult (alcoholic) has occurred from a dose of 1.5 cc., and another from 2 cc., both cases[4] emphasizing the influence of alcohol on the toxicity of the drug. These same authors report deaths of a boy of 7 years and a girl of 5 from doses of 0.3 cc., the former dying in a few hours, while a third case of a boy of 6 proved fatal after a dose of 0.5 cc. In the cases reported by Phelps and Hu[5], death of a child 5½ years followed a dose of 1 cc., and a dose of 3 cc. proved fatal in 40 hours with an adult.

Treatment.—In the handling of carbon tetrachloride poisoning, it is probable that prevention of medicinal poisoning is as important as the later treatment. It follows from what has been previously stated that this drug should not be administered without preparation of the patient. A patient infested with round worms, as well as with hookworms, should not be given carbon tetrachloride without preliminary treatment for the ascaris infestation; alcoholics should not be treated with this drug; the patient should avoid alcohol or food (especially fatty food) shortly before or after the administration of the drug; and, lastly, an adequate calcium reserve should be built up in all persons treated. It is probably true that most normal adults and children have a sufficient calcium reserve to prevent the toxic action of the ordinary doses of carbon tetrachloride, but the poorly nourished individual must receive, for some time prior to the treatment, adequate calcium, either in the food or in the calcium salts. The calcium may be administered by mouth, probably, the best, as well as the most rapid and effective method of increasing available calcium in the blood, providing it can be retained by the stomach. The chief objection to this oral administration is the possible lack of absorption, especially from the alkaline intestinal contents. For this reason it has been found that administration of hydrochloric acid serves to increase the available blood calcium by promoting its absorption, as well as by making the stored calcium available. Much the same effects are produced by administration of ammonium chloride. The patient should be watched for signs of acidosis, manifested by air hunger, as a sign that such medication has been pushed far enough. Administration of parathyroid extract may, also, be used in the effort to raise the blood calcium. Intravenous introduction of calcium should not be employed, unless the patient is moribund, when the chance may be taken that the injection may not result in a hypercalcemia.[1]

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[1] See Lamson and McLean, Jour. Pharm. and Exp. Therap., 1923, **21**, 237; Lamson, Gardner, Gustafson, Maire, McLean, and Wells, Ibid., 1923, **22**, 215; Smillie and Pessoa, Amer. Jour. Hyg., 1923, **3**, 35; Taylor, Jour. Amer. Med. Assoc., 1925, **84**, 280.

[2] See Schultz and Marx, Amer. Jour. Trop. Med., 1924, **4**, 469; Minot, Proc. Soc. Exp. Biol. and Med., 1927, **24**, 617; Lamson, Minot, and Robbins, Jour. Amer. Med. Assoc., 1928, **90**, 345; Minot and Cutler, Jour. Clin. Inves., 1928, **6**, 369.

[3] See Wells, Proc. Soc. Exp. Biol. and Med., 1925, **22**, 235.

[4] Lamson, Minot, and Robbins, Jour. Amer. Med. Assoc., 1928, **90**, 345.

[5] Jour. Amer. Med. Assoc., 1924, **82**, 1254.

Postmortem Appearances.—The principal changes noted appear to be a central necrosis of the liver with some fatty infiltration, together with evidence of fatty changes in the kidneys and necrosis of the suprarenal glands. According to Meyer and Pessôa[2], the liver, at autopsy of experimental animals, was bright yellow and lusterless, and traced by yellow lines inclosing darker, depressed areas. Microscopic examination of the liver sections showed necrosis in the central portion of the lobule of the liver, and a zone of fatty infiltration at the periphery of the acini. In the least affected cases, droplets of fat of various sizes in the vicinity of the portal spaces may be observed. The kidneys before section did not appear markedly abnormal, but the cut surface disclosed a brownish yellow zone in the cortex external to which there was a gray band of linear threads radially arranged. The microscopic changes in the kidneys consisted of droplets of fat in the epithelial cells of the loops of Henle and the convoluted tubules. The suprarenal glands show necrosis of cells of the inner portion of the zona fasciculata and of the zona reticularis. MacMahon and Weiss[3] report a case in which the blood in the right side of the heart and larger pulmonary arteries contained as much as 60 per cent. of fat.

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[1] See Lamson, Minot, and Robbins, Jour. Amer. Med. Assoc., 1928, **90**, 345.

[2] Amer. Jour. Trop. Med., 1923, **3**, 177. See, also, Lambert, Jour. Amer. Med. Assoc., 1923, **80**, 526; Phelps and Hu, Ibid., 1924, **82**, 1254; Gardner, Grove, Gustafson, Maire, Thompson, Welland, and Lamson, Bull. Johns Hopk. Hosp., 1925, **36**, 107.

[3] Amer. Jour. Path., 1929, **5**, 623.

Detection.—Carbon tetrachloride is isolated from the tissues by distillation from acid solution, as is chloroform. It gives the phenylisocyanide (isonitril) reaction, but not the naphthol and resorcin tests. It is differentiated from chloroform by the fact that, on heating with alcoholic potassium hydroxide, potassium chloride and potassium carbonate are formed, while chloroform yields potassium chloride and potassium formate under this treatment.

TETRACHLORETHANE

Tetrachlorethane found wide use preceding and during the war as a solvent for cellulose acetate, which was employed in airplane "dope" or varnish, with which the wings and other parts of the planes were treated. It is now used in the manufacture of non-inflammable cinematographic films, lacquered goods, artificial silk, varnishing artificial pearls, etc.

Numerous cases of poisoning arose, during the war, as a result of its use on airplanes, the first cases appearing in Germany[1], but the Germans quickly abandoned its use. In England, however, no substitute was found for it during the early years of the war, so that in 1917 there were reported no less than 70 cases of toxic jaundice from its use, 12 of which were fatal.[2] Apparently no fatal cases have occurred in the United States[3], although this halogen compound must be regarded as a potential industrial menace. Leri[4] has reported the cases of 2 women showing a peculiar form of polyneuritis arising from dipping artificial pearls in a varnish containing a high percentage of tetrachlorethane. Practically all the reported cases of poisoning reported have been of the subacute or chronic type, although individuals may be acutely poisoned if exposed to high concentrations, following such accidents as spilling the material on the clothes.

Properties.—Tetrachlorethane (acetylene tetrachloride, $CHCl_2$-$CHCl_2$) is a heavy, colorless, oily liquid, with a sweet odor similar to that of chloroform, a boiling point of 147.2°C. and a specific gravity of 1.614. It is volatile and yields a vapor that is considerably heavier than air, so that it tends to fall to the lower portions of the working quarters, and does not readily mix with the air of the rooms. It is non-inflammable and, also, affords a waterproof coating when applied in varnishes.

Symptoms.—In a typical case the onset is characterized by a sense of abnormal fatigue, general discontent and nervousness, inability to concentrate, drowsiness, loss of appetite, headache, and insomnia.[5]

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[1] See Jungfer, Zentralbl. f. Gewerbehyg., 1914, **2**, 222; Grimm, Vrtljschr. f. ger. Med., 1914, **48**, II Supp., 161; Heffter and Joachimoglu, Ibid., 192; and Koelsch, Münch. med. Wchnschr., 1915, **62**, 1567.

[2] See Hamilton, Monthly Review, U. S. Bureau of Labor Statistics, 1918, **6**, 289.

[3] Hamilton, Jour. Amer. Med Assoc., 1917, **69**, 2037.

[4] See Paris Letter, Jour. Amer. Med. Assoc., 1923, **80**, 709.

[5] See Parmenter, Jour. Ind. Hyg., 1921, **2**, 456; Minot and Smith, Arch. Int. Med. 1921, **28**, 687.

After days, or even weeks, jaundice develops, and the gastric and nervous symptoms increase, following which there may be confusion, delirium, coma and death. "Besides jaundice, which may become moderate in degree, the important physical signs which develop relatively late, consist chiefly of an occasional palpable and tender liver, general abdominal tenderness, pallor and loss of weight." Minot and Smith[1] have shown that blood examination is of value in the early diagnosis, and, may prove important in the prevention of such poisonings. These authors classify the blood abnormalities as a progressive increase of large mononuclear cells, often reaching 40 per cent; the appearance of many immature large mononuclears; a slight increase in the white count; a progressive but slight anemia; and a slight increase in the number of platelets. They state that "A percentage of large mononuclear white cells above 12 is the first sign of a reaction to tetrachlorethane, and is a signal for the observation of that person."

In the severe or fatal cases Willcox[2] describes the symptoms much as given above. In addition, in these cases, a purpuric rash, hemorrhages, hematemesis, convulsions, and suppression of the urine were noted. The jaundice in these cases of poisoning has been attributed to a cholangitis in the smaller bile-ducts, which condition produces obstruction of the bile. In some of the cases, the nervous symptoms were especially prominent, consisting of tremors, anesthesias, numbness, and excessive sweating. In Leri's cases[3] there was a polyneuritis, characterized by a paralysis affecting chiefly the interosseal muscles of the feet and hands, and, to a lesser degree, the extensor muscles of the feet, and the flexor muscles of the hands; anesthesia in the region of the interosseal branches of the extremities; abolition of all the tendon reflexes; paralysis of the soft palate, associated with suppression of the pharyngeal reflex, and paralysis of the orbicularis oculi and orbicularis oris.

Fatal Dose.—There is not much information upon which one may base an opinion as to the fatal quantity of tetrachlorethane. This liquid is, when vaporized, much more fatal than are either chloroform or carbon tetrachloride. Thus, it has been found[4] that a concentration of 7300 parts of tetrachlorethane in a million of air is rapidly fatal for short exposures, while 25,000 parts of chloroform and 48,000 to 63,000 parts of carbon tetrachloride per million of air prove fatal for such short exposures. The hemolytic power of tetrachlorethane is about 7 times as marked as that of chloroform, according to Benzi.[5]

Treatment.—Prophylaxis should be instituted in the form of proper ventilation of working quarters and careful medical control, with weekly blood examinations. When affected, the subject should be promptly removed from exposure and should be given plenty of rest. Administration of alkalies seems to be of value in some cases. The bowels should be kept well open with salines. Return to work should not be permitted for at least a month after the jaundice has disappeared.

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[1] *Loc. cit.*

[2] Lancet, 1915, **1,** 544.

[3] *Loc. cit.*

[4] See Herrmann, Inaug. Dissert, Würzburg, 1911; Lehmann, Arch. f. Hyg., 1911, **74,** 1.

[5] Boll. d. soc. med.-chir. de Pavia, 1925, **37,** 537; Abs. in Ber. d. ges. Physiol., 1926, **35,** 179.

Postmortem Appearances.—The liver shows a marked fatty degeneration, in some cases resembling the changes noted in phosphorus poisoning and acute yellow atrophy. The kidneys, also, show fatty changes, but these do not appear to be as characteristic as those in the liver.

ALCOHOLS

The alcohols are formed by replacement of one or more hydrogens of the hydrocarbons by the hydroxyl (OH) group, the hydrogen atoms replaced being attached to different carbon atoms. The resulting derivatives are known as monohydric, dihydric, trihydric, tetrahydric, pentahydric, hexahydric and polyhydric alcohols, and show a decreasing toxicity with the number of hydroxyl groups introduced.

In the series of normal monohydric alcohols, the toxicity, as a rule, increases with the molecular weight, but an exception must be made in the case of methyl alcohol, which appears to be slightly more toxic to man than ethyl alcohol, although with animals it is slightly less toxic[1]. The monohydric alcohols are classified as primary, secondary, or tertiary, according as 1, 2, or 3 of the valencies of the carbon atom bearing the hydroxyl group are bound to alkyl radicals. Of such isomeric monohydric alcohols the primary is usually more harmful than the secondary, and this latter, in turn, less toxic than the tertiary form, although there are exceptions to this rule, the primary isoamyl alcohol, for instance, being, probably, more dangerous than the tertiary amyl alcohol.

METHYL ALCOHOL

Methyl alcohol is obtained by the destructive distillation of wood or molasses, and occurs in commerce in different states of purity. The crude wood alcohol contains, among other substances, such impurities as acetone, ethyl-methyl ketone, methyl and dimethyl acetate, furfural, and allyl alcohol. In its purified state it is found under such names as "Columbian spirits", "Colonial spirits", and "Eagle spirits". Methyl alcohol finds rather wide use in the arts as a solvent for fats, oils, and, especially, for resins and varnishes. It has been employed as a substitute for ethyl alcohol in the preparations of such articles as essences of Jamaica ginger and peppermint, and of bay rum, and is widely used as a denaturant of ethyl alcohol, from which sources many cases of poisoning have arisen. It is of interest that methyl alcohol may be found in certain home-made wines, and, especially, in those prepared from the grape skins (the so-called "after wine"), the decomposition of the pectin substances leading to its formation. Further, methyl alcohol appears to be formed in small quantities by the action of many types of yeast upon saccharine fluids, the quantity being increased by the addition of glycocoll to the culture medium[1].

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[1] See Macht, Jour. Pharm. and Exp. Therap., 1920, **16**, 1; and Munch and Schwartze, Jour. Lab. and Clin. Med., 1925, **10**, 985.

Poisoning with methyl alcohol was almost unknown prior to 1898, but has become somewhat extensive since that time. The avenues of entrance of the poison into the system seem to be varied. Thus, blindness has resulted from its external application as a body rub[2], and many cases have arisen from its inhalation by workmen using varnishes or shellacs dissolved in this solvent, Baskerville[3], for instance, reporting 64 cases from this source. Hamilton[4] states that "In industrial cases the very severest forms of wood alcohol poisoning have been seen, especially among men who use varnish with this solvent in small airless spaces." She further says, "Methyl alcohol is especially an American poison, and it has probably done more damage in the United States than in all other civilized countries put together." Possibly, the most frequent and, probably, the most dangerous source of poisoning is the drinking of the pure methyl alcohol, or of alcoholic beverages or products containing this alcohol as an impurity. The earlier reports indicated the drinking of such preparations as essence of Jamaica ginger, peppermint, cinnamon, vanilla, and lemon extracts, bay rum, etc., or of "Columbian spirits" as the cause of the poisoning[5], these cases coming, largely, from so-called "prohibition" districts. In 1904 Buller and Wood[6] collected 275 cases of methyl alcohol poisoning, of which 122 died and 153 became blind, while Baskerville[7] in 1913 collated 725 cases, of which 390 died, 90 became totally blind, 85 showed impaired vision, and in about 100 the results were not specifically stated. Many cases of "mass poisonings" have occurred in Russia, Hungary, United States, and elsewhere. Thus, Ströhmberg[8] reports 51 deaths in Russia, while Stadelmann and Magnus-Levy[9] record the poisoning of about 174 individuals in Berlin, of whom 80 died, 42 became blind or showed impaired vision, and 32 recovered. Since the use of wood alcohol as a denaturant of ethyl alcohol has become so wide spread in the United States, the number of deaths from this cause have been many, although it is probably true that relatively few of the deaths from alcohol can be charged against adulteration with wood alcohol, as many other factors enter into consideration.

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[1] See Takahashi, Gunke, and Yamazaki, Jour. Amer. Chem. Soc., 1917, **39,** 2723, and Fellenberg, Biochem. Ztschr., 1918, **85,** 45.

[2] See Woods, Jour. Amer. Med. Assoc., 1913, **60,** 1762.

[3] Second Report, Factory Investigation Com., New York, 1913, **2,** 921. See, also, Patillo, Ophthalmic Rec., 1899, **8,** 599; de Schweinitz, Ibid., 1901, **10,** 289; Hale, Jour. Amer. Med. Assoc., 1901, **37,** 1450; Wood, Ibid., 1912, **59,** 1962; Loewy and von der Heyde, Biochem. Ztschr., 1914, **65,** 230; and Ziegler, Jour. Amer. Med. Assoc., 1921, **77,** 1160.

[4] *Industrial Poisons in the United States,* 1925, p. 419.

[5] See Thompson, Proc. Phila. Med. Soc., 1897; Wood, Ophthalmic Rec., 1899, **8,** 55; and MacCoy and Michael, Med. Rec., 1898, **53,** 777.

[6] Jour. Amer. Med. Assoc., 1904, **43,** 972, 1058, 1117, 1213, and 1289.

[7] *Loc. cit.*

[8] Petersb. Med. Wchnschr., 1904, **31,** 55.

[9] Berl, klin. Wchnschr., 1912, **49,** 193.

Properties.—Pure methyl alcohol (methanol, carbinol, wood alcohol, pyroligneous spirit, CH_3OH) is a colorless, mobile liquid, with a spirituous odor and a pungent, burning taste. It mixes readily with water, ethyl alcohol and ether. It has a specific gravity of 0.8021 at 15.56°C., and boils at 66°C. It is oxidized into formaldehyde, formic acid, and, finally, into carbon dioxide.

Symptoms.—The symptoms of poisoning by methyl alcohol appear more slowly and last much longer, as a rule, then those due to ethyl alcohol, due, probably, to the fact that the oxidation of methyl alcohol proceeds quite slowly and that both the alcohol itself and its oxidation products are retained in the system for a long period, while ethyl alcohol is relatively quickly oxidized and its oxidation products rapidly excreted. In animal experiments it appears that, when given in single dose, methyl alcohol is slightly less poisonous than ethyl alcohol, but, when the administration is repeated, methyl alcohol becomes more toxic than ethyl alcohol, on account of the slower oxidation and more prolonged action in the case of methyl alcohol.[1]

In many of the cases there is a "latent" period following the taking of the methyl alcohol, which may vary from a few hours to days, the subjects being, often, able to continue their work for some time before symptoms appear. Rarely do marked symptoms of true intoxication or "drunkenness" obtain, although this alcohol must be regarded as intoxicating. In some of the cases the symptoms appear suddenly in severe form, the patient seeming to be struck down and rapidly becoming unconscious, passing into deep coma, with cyanosis, failing respiration, and cold sweats, with death coming within a short time (½ hour) after the beginning of the symptoms. In other cases, however, the course is more prolonged. There is depression, weakness, headache, nausea, severe pain in the epigastrium, marked dyspnea, cyanosis, cold sweats, convulsive seizures, delirium (or, in some cases, stupor), dilated pupils, which do not react to light, collapse, coma, and death. Not all cases show the comatose state, while others may be associated with a coma that lasts for several days before death, or, occasionally, recovery. The urine of the subject will show large amounts of formic acid. There is a condition of general acidosis, as evidence of profound alteration in the general metabolism, although the complex of poisoning is, certainly, not that of a simple acid intoxication.

The most frequent and important single symptom of methyl alcohol poisoning is blindness, which occurs in a large percentage of severe cases, and in some cases is practically the only symptom observed.[1] This may appear in a few hours or be delayed for several days, some cases being comatose for days and then awaking blind. This blindness is bilateral, and is due to atrophy of the optic nerve.[2] There is, in the beginning, a feeling of pain about the eyes, and tenderness on pressure over the lids, slight photophobia, dilatation of the pupil, followed by blurred vision, and, after a variable period, blindness, which may be partial or complete. Occasionally, cases are seen in which apparent recovery of sight is noted, but, in a few days or weeks, vision is again lost. Burnett[3] reports that in some cases the color sense is chiefly affected.

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[1] See Hunt, Bull. Johns Hopk. Hosp., 1902, **13**, 213; and Sollmann, Jour. Pharm. and Exp. Therap., 1920, **16**, 291.

Chronic poisoning with methyl alcohol is quite important from a medical point of view. Especially to be considered are the eye symptoms and various disturbances of the nervous system, especially the local and general neuritis, which is not uncommon. The prognosis of the eye condition can not be accurately given for months, because, following a preliminary improvement, a relapse with possible blindness may obtain. After repeated intake or inhalation of methyl alcohol, a tolerance may be established, so that the excretion of formic acid in the urine may be appreciably lessened, although Leo[4] was able to offer no entirely satisfactory explanation for this.

Fatal Dose.—Individuals differ markedly in their reaction to the effect of methyl alcohol, some showing a hypersensibility (idiosyncrasy), while others are somewhat tolerant. On this account, the fatal dose can not be stated definitely. Franceschi[5] took 32 grams of pure methyl alcohol daily for 274 days without suffering ill effects. The fatal dose for man appears to be somewhere between 30 and 100 grams, although Kobert[6] places this between 120 and 240 grams. A tablespoonful has caused convulsions and death[7], while 30 to 60 cc. have, also, proven fatal[8]. Swadener[9] has reported the cases of 4 Indians, each of whom drank 4 ounces of methyl alcohol; 2 died on the third and fourth day; 1 was comatose for 3 days and recovered, although he was blind; while the fourth showed few symptoms. Doses of 150 to 250 cc. have often caused death, but recovery has followed the intake of larger quantities. Doses as low as 15 cc. have caused blindness, while much larger amounts have been taken without causing either temporary or permanent eye trouble.

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[1] See Harlan, Ophthalmic Rec., 1901, **10**, 81; and Gifford, Ibid., 342.

[2] See Birch-Hirschfeld, Arch. f. Ophthal., 1902, 54, 68; Uhthoff, Graefe-Saemisch Handbuch, 1907, **5**, 11; Hirschberg, Berl. klin. Wchnschr., 1912, **49**, 247.

[3] Ophthalmic Rec., 1902, **11**, 309.

[4] Biochem. Ztschr., 1927, **191**, 423.

[5] Cited by Rost and Braun, Arb. d. Reichsgesundheitsamtes, 1926, **57**, 580.

[6] *Lehrbuch der Intoxikationen*, 2te. Aufl., 1906, p. 663.

[7] Zangger, "Die organischen Gifte," in *Lehrbuch der Toxikologie* by Flury and Zangger, 1928, p. 179.

[8] Pierce, Boston Med. and Surg. Jour., 1909, **160**, 232; and Swadener, Jour. Amer. Med. Assoc., 1913, **60**, 1479.

[9] *Loc. cit.* See, also, Moulton, Ophthalmic Rec., 1899, **8**, 335.

Fatal Period.—According to Lewy[1] death may occur within ½ hour, and Hunt[2] states that it is reported to have followed after 1 hour, but, usually, it occurs in from 24 to 36 hours.

Treatment.—The stomach should be washed out repeatedly. Stimulants, such as caffeine and camphor, may be beneficial. The body should be kept warm with hot packs. Diuresis should be stimulated by injection of Ringer's solution or normal saline. Morphine may be necessary to control the pain. Alkalies, by mouth or intravenously, may be used to combat the acidosis[3], although Hunt[4] doubts the value of this treatment. Pohl[5] recommends the subcutaneous injection of sterile yeast. For the eye symptoms, pilocarpine and potassium iodide seem to be of some value in the early stages, while strychnine may have some influence in the later stages.

Postmortem Appearances.—There is usually cyanosis of the head and face. Rigor is well marked. The blood and the lividities are brighter red than is usual, leading one to think of carbon monoxide poisoning[6], but this has been shown[7] not to be present. There are hyperemia and superficial hemorrhages of the mucous membranes of the stomach and duodenum. The lungs are hyperemic and edematous, and the bronchi may be covered with a thick mucus. The brain and meninges are edematous and congested, while the spinal fluid may be increased in quantity. The ganglion cells of the spinal cord, sympathetic ganglions of the neck, trunk, and retina, nerve plexuses of the heart and alimentary organs, main trunks of such nerves as the pneumogastric and optic, and important centers of the pons and medulla, all show different phases of necrosis[8]. Hyperemia of the bladder mucosa appears to be a more or less constant finding. The liver may be enlarged and fatty.

Detection.—Methyl alcohol is, as has been stated above, more difficultly oxidized than is ethyl alcohol. For this reason it is, often, possible to detect methyl alcohol itself in the tissues for a few days after its intake, only about 40 per cent. of the methyl alcohol being oxidized in 48 hours. While much of the ingested wood alcohol may be eliminated by the breath, in which it may be detected for a week, considerable of this alcohol is oxidized slowly to formic acid and escapes in the urine, the elimination being slow and continuing for several days[9]. It follows, therefore, that the diagnosis of methyl alcohol poisoning is made, during life, by the examination of the urine for formic acid, while, after death, both this acid and methyl alcohol itself may be found in the blood and tissues. It must be remembered, in this connection, that a qualitative test is no criterion of a methyl alcohol poisoning, as the urine normally contains a small amount of formic acid, so that a quantitative test must be made in all suspected cases. According to Autenrieth[1] a person, on the average, eliminates 0.251 gram of formic acid in 24 hours, while there is a marked increase following intake of methyl alcohol.

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[1] Dissertation, Berlin, 1912.

[2] "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 609.

[3] See Gettler and St. George, Jour. Amer. Med. Assoc., 1918, **70**, 145; Harrop and Benedict, Ibid., 1920, **74**, 25; and Isaacs, Ibid., 1920, **75**, 718.

[4] *Loc. cit.*

[5] "Organische Gifte" in *Toxikologie* by Starkenstein, Rost and Pohl, 1929, p. 290.

[6] See Ströhmberg, St. Petersb. med. Wchnschr., 1904, **31**, 55 and 421.

[7] Fujiwara, Vrtljschr. f. ger. Med., 1921, **62**, 215.

[8] See Mogilnitzkie, Deutsche Ztschr. f. d. ges. ger. Med., 1927, **9**, 302.

[9] See Asser, Ztschr. f. exp. Path. und Ther., 1914, **15**, 322.

Determination of Formic Acid in Urine.—The method recommended is a combination of the procedures of Scala[2] and of Lieben.[3] This is based upon the fact that mercuric chloride is reduced by formic acid to mercurous chloride, which may be weighed and the amount of formic acid calculated. As other substances, especially aldehydes, may be volatilized in the process, and will, also, reduce the mercuric chloride, separation of the formic acid is brought about by treating the distillate with calcium carbonate and evaporating to a small bulk[4].

Place 300 cc. of the suspected urine in a 750 cc. distilling flask and add 30 cc. of 25 per cent. phosphoric acid and a few pieces of pumice stone to prevent bumping. Begin the distillation with a small flame, as frothing may be intense at the start of the distillation. After the mixture has boiled for 10 or 15 minutes, increase the flame and boil vigorously, collecting the distillate in a graduated cylinder. When about 300 cc. (but no more) have passed over, stop the distillation and add 30 cc. of water to the flask. Distill off 30 cc. and repeat the same process until the distillate fails to show an acid reaction, a point which is not reached until about 1500 cc. have been distilled. Now add an excess of calcium carbonate suspended in water to the distillate, and pour the neutralized distillate into a larger evaporating dish. Bring rapidly to a boil and evaporate on the water-bath to a volume of 20–30 cc. Filter, rinse the dish with a little hot water and wash the filter several times with hot water, allowing the filtrate to run into an Erlenmeyer flask. Now add 50–60 cc. of cold saturated mercuric chloride solution. Heat for 5 to 6 hours in the water-bath under a reflux, shaking the flask frequently. Add 2 to 3 cc. of 20 per cent. hydrochloric acid, shake, and warm 10 minutes longer in the water-bath. Filter the precipitated mercurous chloride through a weighed Gooch crucible, wash with water until the filtrate is free from chlorine, following the water with alcohol and, then, with ether, dry at 100–110°C., and weigh. If the weight of the calomel be multiplied by 0.0977 the result will be the amount of formic acid in the quantity of urine taken for examination.

Isolation of Methyl Alcohol from Tissues.—Methyl alcohol may be isolated from the tissues by distillation in a boiling water-bath with steam. In this process there is, often, considerable frothing of the material, and, also, there is some danger of over-heating the mixture. For this reason Juckenack[1] recommends distillation from an oil bath, the temperature being slowly raised to about 150°C., sodium chloride being added to raise the boiling point of the mixture, and the distillation continued until the weight of the distillate obtained is about half that of the comminuted tissue taken. The tests to be employed for the recognition of the methyl alcohol in this distillate are, obviously, different from those to be used in the identification of pure methyl alcohol itself, as we are dealing with very dilute solutions. Such tests depend upon the oxidation of the methyl alcohol to formaldehyde, so that the distillate must be tested, before treatment, for the presence of formaldehyde by the tests outlined under this substance. There are several methods of oxidizing the methyl alcohol, such as the use of a copper spiral brought to a red heat; the employment of sulphuric acid and potassium dichromate and distilling; and the use of potassium permanganate and sulphuric acid or phosphoric acid[2], the writer preferring the Pharmacopoeial method, which is practically that of La Wall[3], which in turn is a modification of an earlier one of Denigès[4].

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[1] Münch. med. Wchnschr., 1919, **66**, 862

[2] Gazz. chim. Ital., 1860, **20**, 393.

[3] Monatsh. f. Chemie, 1893, **14**, 747.

[4] See Autenrieth-Warren, *Detection of Poisons*, 1928, p. 98.

Oxidation Method for Methyl Alcohol.—In a test tube of about 20 cc. capacity place 5 cc. of the distillate from the tissues, add 0.5 cc. of syrupy (85 per cent.) phosphoric acid and 2 cc. of a 3 per cent. aqueous solution of potassium permanganate, and allow the mixture to stand for 10 minutes. Now add 1 cc. of an aqueous 10 per cent. solution of oxalic acid and allow to stand until the liquid is a transparent brown. Add 5 cc. of a diluted and cooled sulphuric acid (prepared by mixing 3 volumes of distilled water and 1 volume of concentrated sulphuric acid), add 5 cc. of freshly prepared fuchsin-sulphurous acid solution[5], mix well, and allow to stand for 10 minutes. If formaldehyde is present a distinct blue or violet color will appear, while a reddish or pale green tint may be shown in the absence of formaldehyde, or, in other words, in the absence of methyl alcohol in the original distillate.

Autenrieth's Test.—This test does not depend upon the oxidation of methyl alcohol to formaldehyde, but, rather, upon the formation of methyl ester of p-brom-benzoic acid, which is distinctly crystalline, while the ethyl ester, which may be formed if ethyl alcohol is also present, remains liquid at the temperatures employed.[6]

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[1] Ztschr. f. Unters. d. Nahrungs.-und Genussm., 1912, **24**, 7.

[2] See Gettler, Jour. Biol. Chem., 1920, **42**, 311; and Jansch, Vrtljschr. f. ger. Med., 1921, **62**, 1.

[3] Amer. Jour. Pharm., 1923, **95**, 812.

[4] C. R. Acad. des Sciences, 1910, **150**, 529.

[5] This is known as Schiff-Elvove Reagent and is prepared as follows: Dissolve 0.2 gram of basic fuchsin in 120 cc. of hot distilled water, cool the solution, add a solution of 2 grams of anhydrous sodium sulphite in 20 cc. of distilled water, and follow by 2 cc. of concentrated hydrochloric acid. Dilute this solution with distilled water to 200 cc. and allow to stand for 1 hour before use. This solution should be prepared every few days, as it is prone to lose its properties on standing.

[6] Arch. der Pharm., 1920, **258**, 1.

Place 40 or 50 cc. of the distillate obtained as outlined above in a glass-stoppered flask, add 10 cc. of a 10 per cent. solution of sodium hydroxide, and warm the mixture to 40° to 45°C. According to the quantity of methyl alcohol suspected add 1 to 5 grams of ground p-brom-benzoyl-chloride, and shake vigorously until the mixture is cold. It is important that the mixture remain alkaline, so that, if the reaction becomes acid (as tested by litmus paper), more sodium hydroxide should be added. In the presence of methyl alcohol, the methyl ester of p-brom-benzoic acid separates as a white, usually friable powder. This is filtered off, washed with cold water until free from alkali, and dried upon a porous plate or in a vacuum desiccator, after which it may be crystallized from alcohol, methyl alcohol or acetone, settling out from alcohol in the form of shining leaflets, from methyl alcohol in fine needles. This methyl ester of p-brom-benzoic acid has an anise-like odor, and melts sharply between 78° and 79°C.

If this test is to be employed, the tissues should be first distilled from acid solutions, to hold back any ammonia formed in the putrefactive processes, and then the distillate should be alkalinized with sodium hydroxide and redistilled, providing the first distillate gives a reaction for phenols with such tests as Millon's reagent. If this precaution be neglected, interfering reactions will be introduced from the presence of ammonia and phenols.

Detection of Pure Methyl Alcohol.—In the usual toxicological tests the methyl alcohol is obtained in dilute solution in the distillate, and the tests applicable to the detection of methyl alcohol in larger amounts are rarely carried out. If one wishes to determine the presence of methyl alcohol in ethyl alcohol, the above tests may be employed with accurate results. If occasion should arise for testing supposed methyl alcohol, and a few cc. of the alcohol itself are available, one may employ the method of Riche and Bardy,[1] of Windisch[2], of Trillat[3], and the determination of the specific gravity, degree of refraction by the immersion refractometer, and other tests, for the details of which we refer to other works[4]. A good quantitative micro method for methyl alcohol has been outlined by Chapin[5].

ETHYL ALCOHOL

"From almost every standpoint", says Hunt[6], "ethyl alcohol must be regarded as the most important poison with which medical men and

[1] C. R. Acad. des Sci., 1875, **80,** 1076.

[2] Arb. aus dem Kais. Gesundheitsamte, 1893, **8,** 286.

[3] C. R. Acad. des Sci., 1898, **127,** 232; **128,** 438.

[4] See Hunt and Gettler, "Non-alkaloidal Organic Poisons" in *Legal Medicine* and *Toxicology* by Peterson, Haines and Webster, 1923, **2,** 610; and Official and Tentative Methods of Analysis of the Association of Official Agricultural Chemists, 2nd edition, 1925, p. 372.

[5] Jour. Ind. and Eng. Chem., 1921, **13,** 543. See, also, Kistler, Science, 1929, **69,** 457.

[6] *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2,** 613.

jurists have to deal; no other poison causes so many deaths or leads to or intensifies so many diseases, both physical and mental, as does alcohol in the various forms in which it is taken." Alcohol, in the form of some type of beverage, has been known from the earliest times, each country having some national drink containing it. Alcoholic drinks are, ordinarily, prepared by the fermentation of sugars or starches by yeasts, the wines and beers containing a relatively low percentage of alcohol, while the spirits, being distilled products, show a higher alcohol content. In this fermentation are produced, however, other products, such as acetal, aldehydes, acetone, succinic acid, glycerin, furfurol, amyl alcohol, etc. The beers run from 1 to 5 per cent. alcohol, the wines from 5 to 20 per cent., and the spirits (whisky, brandy, rum, gin, arrak, etc.) from 45 to 60 per cent. The official preparations of alcohol are *Alcohol* (92.3 per cent. by weight), *Alcohol Dehydratum* (absolute alcohol, 99 per cent. by weight), *Alcohol Dilutum* (41 per cent. by weight), *Spiritus Frumenti* (whisky, 47 to 53 per cent. by volume), and *Spiritus Vini Vitis* (brandy, 48 to 54 per cent. by volume.

It is impossible to give any exact figures as to the number of deaths from acute alcoholism, especially in relation to the total number of actual cases of intoxication, as no satisfactory data are at hand. There seems to be little doubt, however, that the number of cases, both of non-fatal and fatal types, of alcoholism is increasing. Thus, Gerty[1] gives the following table of alcoholics admitted to the Cook County Hospital in Chicago for a period of years preceding and following the adoption of the 18th Amendment.

Year	*Alcoholics*
1910	387
1911	422
1912	827
1913	486
1914	225
1915	140
1916	99
1917	199
1918	149
1919	168
1920	641
1921	911
1922	1130

The mortality statistics of the Chicago Health Department, also cited by Gerty, show the following: 187 deaths from alcoholism in 1917; 46 in 1920; 155 in 1922; and in the first 9 months of 1923 as many as in the entire year 1922. In the figures from the Coroner's Office of Cook County given by McNally[2], it is clear that deaths from alcoholism are increasing, only those cases being given in which a history of alcoholism was obtained or chemical examination proved its existence.

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[1] Ill. Med. Jour., 1924, **46**, 141; Amer. Jour. Pub. Health, 1924, **14**, 603.

[2] Jour. Amer. Med. Assoc., 1924, **83**, 1680.

Year	*Alcoholism*
1910	215
1911	76
1912	108
1913	66
1914	91
1915	110
1916	87
1917	88
1918	46
1919	55
1920	41
1921	97
1922	158
1923	180

In New York City 680 deaths from alcohol were reported in 1916; 84 in 1920; 585 in 1925; and 617 in 1926[1].

As there is much factitious, adulterated, illicit, denatured, and so-called "moonshine" liquor available at the present time, it might be expected that there would be an increase in the number of cases of alcohol poisoning from such sources. It is admitted, of course, that alcoholic beverages denatured with wood alcohol are causing many deaths, but, in reality, the number of such cases are relatively few compared with the total number of cases of poisoning arising from the drinking of the present-day alcohol. Chemical analysis of most of the specimens, which have been responsible for many of the deaths, has failed to show, however, the presence of a definite toxic substance that might be accountable for the increase in the deaths noted. Although there are a large number of denaturants used in alcohol and alcoholic beverages, and an increase of aldehydes or fusel oil is noted in many of the specimens, yet the general opinion held by most workers in this line is that the danger is due to the excessive use of alcohol, when opportunity offers, rather than to the presence of a toxic substance other than alcohol itself[2]. Some individuals do, probably, have a lessened tolerance to ethyl alcohol, owing to the somewhat infrequent use of alcoholics under prevailing conditions, so that an excess may easily be imbibed when occasion presents. Others may show toxic effects from partaking of highly concentrated alcoholics, such as various essences, toilet waters, liquid from "canned heat", etc. The symptoms, especially the psychoses observed, may be, in many cases, quite different from those noted in pre-Volstead days.

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[1] See Reports of the Chief Medical Examiner of the City of New York for these years.

[2] See McNally, Jour. Amer. Med. Assoc., 1924, **83**, 1680; Gerty, Amer. Jour. Pub. Health, 1924, **14**, 603; Bigelow, New England Jour. of Med., 1928, **198**, 227; Lythgoe, Ibid., 228; Hunt, Ibid., 230; Atkinson, Jour. Amer. Pharm. Assoc., 1928, **17**, 28; Howard, New England Jour. of Med., 1929, **200**, 933.

While practically all of the alcohol poisonings arise from drinking of some form of it, yet cases of death have occurred from rectal injection of whisky, from long continued exposure to alcohol in industries, and from inhaling the vapor in cases in which children have been wrapped in cloths soaked in alcohol[1].

Properties.—Alcohol (ethanol, ethyl alcohol, C_2H_5OH) is a transparent, colorless, mobile, volatile liquid, having a characteristic odor, and a burning taste. It is very hygroscopic, has a specific gravity not above 0.798 at 15.56°C., and boils at about 78°C. It ignites readily, burning with a non-luminous flame. On oxidation it is converted into acetaldehyde and acetic acid. As found in commerce it contains a variable amount of water and other impurities.

Absorption and Elimination.—When alcohol is taken into the stomach, it is absorbed rapidly, about 20 per cent. being taken up from the stomach and 80 per cent. from the small intestine. The rate of absorption varies with the concentration of the alcohol, the researches of Miles[2] showing that the same weight of alcohol taken in a concentrated solution produces a definitely higher alcohol concentration in both blood and urine than when taken in a more dilute form. Thus, when taken in a concentration of 2.75 per cent., the amounts in the venous blood at 20, 40, 70 and 120 minutes after ingestion are 18, 24, 30, and 30 mg. of alcohol per 100 cc., the corresponding values for the urine being 15, 37, 47, and 43 mg. per 100 cc. When ingested in a concentration of 27.5 per cent., the amounts in the blood at the above intervals are 28, 42, 43 and 36 mg., the figures for the urine being 24, 51, 65, and 49 mg. per 100 cc. On the other hand, the work of Tuovinen[3] indicates that the absorption of 4–10 per cent. alcoholic solutions is much quicker than that of the stronger solutions, as shown by the alcoholic content of the blood. Absorption is retarded by the simultaneous taking of food, especially of the fatty types.

A further factor in the rate of absorption is the tolerence of habituation of the individual to alcohol. Thus, Pringsheim[4] shows that normal animals absorb 20 per cent. more alcohol in the first 2 hours than do alcoholic animals, and that normal animals reach a 66 per cent. higher alcoholic content in the blood than habitues. These findings have been confirmed for man by Schweisheimer[5], who shows that the maximum alcohol content of the blood is higher in normal persons; that it reaches this maximum in from 1½ to 2 hours, remaining at this level for 5 hours, and then gradually diminishing; while in alcoholics the blood concentration reaches its maximum more quickly, remains at this level for 2 hours, and then subsides much more quickly. It is probable that this tolerance may be due to more rapid oxidation of the alcohol in habitues, as has been shown by several workers[1]. Pringsheim, for instance, shows that habituated animals burn up the alcohol in about ⅔ of the time taken by normal animals; while Schweisheimer indicates that normal persons get rid of all the alcohol in 7½ hours, and alcoholics destroy it in about ½ of that time. In his later work Schweisheimer[2] found that long-continued habituation (10 to 20 years) may result in the loss of the acquired ability to oxidize alcohol rapidly, and then the person may be much more affected by alcohol than is the abstainer.

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[1] See *Toxikologie* by Starkenstein, Rost and Pohl, 1929, p. 294.

[2] Jour. Pharm. and Exp. Therap., 1922, **20**, 265. See, also, Mellanby, Med. Research Comm., London, Special Report, No. 31, 1919.

[3] Skand. Arch. f. Physiol., 1927, **51**, 287; Abstract in Chem. Abs., 1928, **22**, 2619.

[4] Biochem. Ztschr. 1908, **12**, 143.

[5] Deutsches Arch. f. klin. Med., 1912, **109**, 271.

After absorption of the alcohol, it passes to all the tissues and fluids of the body, the concentration in these different organs being approximately the same[3]. From what has been said, it is clear that a maximum concentration will be reached within 1½ to 2 hours, so that examination of the blood or urine will give us a means of following the course of the intoxication. The work of Miles[4] and of Southgate and Carter[5] has shown that the percentage of alcohol in the blood and the urine runs somewhat parallel, although the urine shows slightly higher figures from 1 to 6 hours after the ingestion, a ratio of 1:1.34 prevailing for the alcohol in blood and urine respectively.

Under ordinary conditions between 90 and 95 per cent. of the ingested alcohol undergoes oxidation in the body to carbon dioxide and water[6]. The amount of alcohol excreted in the urine rarely exceeds 3 per cent., while a small amount is excreted by the lungs[7]. It is probable that the excretion by the lungs is increased by muscular exertion and the consequent hyperpnea, while that passed with the urine may be increased by diuresis. Excretion and oxidation of ethyl alcohol proceed somewhat rapidly, so that after 24 hours only faint traces will be found in the blood and tissues, the rate of absorption and elimination of alcohol being somewhat uniform in different individuals. Probably, the amount excreted by the urine or the pulmonary air increases with habitual indulgence in alcohol[8].

Normal Alcohol.—It is probable that alcohol must be regarded as a normal constituent of the fluids and tissues of the body, although the amount present is trivial as shown by the figures given by the various workers. Thus, Ford[1] found in the blood and organs of different animals an alcohol content ranging from 0.0002 to 0.0015 per cent; Nicloux[2] reported the presence of 0.0018 per cent. of alcohol in dog's blood and 0.001 per cent. in guinea-pigs; Landsberg[3] finds 0.0028 to 0.0083 per cent. in rabbit muscle; Maignon[4] from 0.0015 to 0.0031 per cent. in dog's blood; Pringsheim[5] 0.0023 to 0.0044 per cent. in tissues of rats and 0.0018 per cent. in rabbit's blood; Schweisheimer[6] 0.0030 to 0.00368 per cent. in human blood; Völtz and Dietrich[7] 0.0023 to 0.003 in tissues of dogs; Lenoble and Daniel[8] 0.002 in human cerebrospinal fluid; Kuhn[9] 0.0021 in human blood; Heilner[10] 0.003 to 0.084 in human urine; Aoki[11] 0.002 to 0.003 per cent. in blood of rabbits and 0.0025 in blood of fowls; Gettler and Tiber[12] 0.0006 to 0.0023 per cent. (average 0.00157 per cent.) in human brain; McNally, Embree and Rust[13] 0.0009 to 0.0052 per cent. in human placenta. It will be seen from the above that the human fluids and tissues contain approximately 0.003 per cent. of alcohol, or, at least, of normal volatile substances which react similarly to alcohol.

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[1] See Rosenfield, *Einfluss des Alkohols auf den Organismus*, Wiesbaden, 1901; Pringsheim, *Loc. cit.;* Schweisheimer, *Loc. cit.;* Hansen, Biochem. Ztschr., 1925, **160**, 291.

[2] Schweiz. Chem. Ztg., 1920, p. 524.

[3] See Grehant, C. R. Acad. des Sci., 1895, **120**, 1154; 1896, **123**, 192; 1899, **129**, 746; C. R. Soc. de Biol., 1896, **48**, 839; 1899, **51**, 808 and 946; 1900, **52**, 894; 1903, **55**, 225, 376, 802, and 1264; Jour. de physiol. et de path. gen., 1907, **9**, 879.

[4] Jour. Pharm. and Exp. Therap., 1922, **20**, 265.

[5] Brit. Med. Jour., 1926, **1**, 463. See, also, Carter, Ibid., 1927, **2**, 333.

[6] See Bodländer, Pflüger's Archiv. f. d. ges. Physiol., 1875, **11**, 122.

[7] According to Cushny (*Pharmacology and Therapeutics*, 9th Ed., 1928, p. 194), the odor of the breath after strong alcoholics are taken arises from the higher alcohols and other by-products present in these, and not from the ethyl alcohol.

[8] See Laufberger, Wochschr. Brau, 1928, **45**, 88: Abs. in Chem. Abs., 1928, **22**, 2790.

Symptoms.—The effects of alcohol vary greatly in different individuals and in the same individual at different times. The symptoms noted depend upon such factors as the quantity and strength of the alcohol taken, the rapidity with which it is taken, the concentration of the alcohol in the blood and tissues, and the tolerance of the individual. In small quantities it generally produces a feeling of euphoria and good-fellowship, along with increased confidence in one's mental and physical powers, a tendency towards braggadocio and exaggerated statements being a prominent feature. In larger quantities the first symptoms are a flushing of the face and hands, and a feeling of warmth, followed by a period of excitement, which varies greatly according to the temperament of the individual, some persons being gay and very talkative, others sentimental, still others bellicose and showing outbursts of anger, while some become quiet and show no excitement, but rather a desire to sleep. There is, at this stage, a loss of self-control and a weakening of the will power. The speech may be brilliant, but, oftentimes, somewhat disconnected, the movements are active, and the individual appears to have little regard for the feelings of others. Nausea and vomiting may be noted, dizziness and mental confusion appear, the speech is slurred and, often, inarticulate, while the gait may be staggering and the movements incoordinated. Finally, the subject passes into a deep, torpid sleep, which may last several hours. As long as the person is at rest, the pupils are contracted, but on being roused the pupils dilate gradually, again contracting in a variable time after the subject is allowed to remain quiet. Very large quantities of alcohol may lead to a deep sleep, without any, or at least very little, preceding excitement. The patient falls into a condition closely resembling that of anesthesia, the respiration is slow and, often, stertorous, the pulse rapid at first, then slow and feeble, the face pale or cyanotic and cold, the eyes injected and staring, pupils contracted or dilated, depending on whether or not the subject has been roused from his lethargy. The body temperature is usually lowered several degrees, temperatures of 83° to 86°F. being often noted, while Hunt[1] states that in one case the rectal temperature sank to 75°F. This condition may last several hours and end in death from respiratory failure. In other cases the stupor may not be so deep and the patient recovers after a time, but may die from an accident, or from pneumonia as the result of exposure. In some of the cases an acute alcoholic insanity or melancholia may develop. In the former state the individual may commit acts of violence, even homicide, while in the latter condition there may be a tendency to suicide.

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[1] Jour. Physiol., 1906, **34**, 430.

[2] See various papers as follows: C. R. Soc. de Biol., 1896, **48**, 841; Ibid., 1900, **52**, 295 and 620; Ibid., 1902, **54**, 754; Ibid., 1904, **57**, 652; Ibid., 1906, **60**, 1034; Ibid., 1906, **61**, 492; Ibid., 1912, **73**, 59 and 177; Ibid., 1913, **74**, 267. Thèse de Paris, 1900.

[3] Ztschr. f. physiol. Chem., 1904, **41**, 505.

[4] C. R. Acad. des Sci., 1905, **140**, 1063.

[5] Biochem. Ztschr., 1908, **12**, 143.

[6] Deutsches Arch. f. klin. Med., 1912, **109**, 271.

[7] Biochem. Ztschr., 1915, **68**, 118.

[8] Bull. et mém. Soc. méd. des hôp. de Paris, 1919, **43**, 809.

[9] Arch. f. exp. Path. u. Pharm., 1924, **103**, 295.

[10] Münch. med. Wchnschr., 1924, **71**, 1422.

[11] Jour. Biochem.(Japan), 1925, **5**, 329; 1926, **6**, 307.

[12] Arch. Path. and Lab. Med., 1927, **3**, 218.

[13] Jour. Biol. Chem., 1927, **74**, 219.

Intoxication.—There seems to be little question that intoxication, due to excessive drinking, is increasing. Just what the reasons for this may be do not concern us here. Not only may this intoxication prove fatal to the one drinking the alcohol, but it may result in fatalities to others, who may be injured in automobile or other accidents. It is pertinent, therefore, to ask whether or not it may be possible to determine chemically this state of intoxication or, as it is more frequently called, drunkenness.

In the beginning of this discussion it must be pointed out that individuals differ greatly in their ability to ingest alcohol without showing the usual classic signs of intoxication, some being markedly affected by small quantities, while others may imbibe relatively large quantities without clinical manifestations of intoxication. The courts have held in several cases that the recognition of drunkenness is simply a matter of observation, about which almost any one may testify without any special expert knowledge. While this may be true in the broad sense, yet it is clear that an individual may be so far under the influence of alcohol as to be a menace to others, if not to himself, without the usual signs of intoxication being observed. When the classic symptoms outlined above are present, the condition may be easily recognized, but such signs do not obtain in all cases. The principal point to be settled in this controversy is what really constitutes drunkenness or intoxication. If we are to accept the rulings of the courts that ½ of 1 per cent. alcohol in a beverage makes it intoxicating, then our definitions of intoxication must be based on the effects of such an alcoholic concentration, and these are known to be very slight. Courts have ruled differently on this question. Thus, in the case of Elkin *v.* Buschner[1], the Pennsylvania courts held that although a man may walk straight, attend to business and give no outward or visible signs of intoxication, yet, if he is so affected by alcohol as to be excited, or not to possess that clearness of intellect which he would otherwise possess, he is suffering from acute alcoholism. A somewhat different interpretation is given by the Ohio courts in the case of Gard *v.* State[2] in holding that a man cannot be considered intoxicated within the meaning of the law of the State, even though the odor of alcohol on the breath, a flushed face, and a disposition to talk loudly and freely are shown, unless it is further shown that he had lost either the control of the faculties . . . or of the muscles of locomotion. These rulings differ in the interpretation of the degree of intoxication, the former being based on the slight effects, while the latter extends to the more pronounced action of alcohol. Purves-Stewart[3] submits the following definition of drunkenness: "A drunken person is one who has taken alcohol in sufficient quantity to poison the central nervous system, producing a temporary disorder of the faculties so as to render him unable to execute the occupation in which he was engaged at the time, thereby causing danger to himself or to others." This is very similar to the definition advanced by the Committee on Tests for Drunkenness of the British Medical Association[4], which is as follows: "The word 'drunk' should always be taken to mean that the person concerned was so much under the influence of alcohol as to have lost control of his faculties to such an extent as to render him unable to execute safely the occupation on which he was engaged at the material time." It is probable that a lay definition of drunkenness is but a relative term, as the standards by which one judges of this condition are quite variable in different individuals.

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[1] "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 616.

It has been shown by many workers that the physiologic and psychologic effects of alcohol are largely dependent upon the concentration of the alcohol in the blood and tissues of the subject. As has been previously stated, alcohol, after its absorption, diffuses quite rapidly throughout the system, so that the concentration of the fluids and tissues at any particular moment is approximately the same. The parallelism of the concentration of alcohol in the tissues and fluids of the body is quite as important a factor to be considered, as is the absolute concentration in the tissues and excretions. It follows, therefore, that, if one

[1] 16 Atl. 102.

[2] 33 Ohio Circuit Courts, 632.

[3] Practitioner, 1928, **120,** 175.

[4] Brit. Med. Jour., Supp., Feb. 19, 1926.

determines during life the concentration of alcohol in the blood or urine, he will have a definite basis upon which to base a conclusion as to the existence of intoxication, even in the presence of individual differences of reaction to alcohol. It is equally obvious that the same basis will obtain, if examination of the tissues of the dead body be conducted upon organs removed from individuals who have died a few hours after ingestion of the alcohol. Of course, such examinations have little value if the individual survives for a period of 15 to 24 hours after taking the alcohol, as the poison will all have been oxidized and excreted in that time. It is true that the literature gives figures for the alcoholic content of the organs and fluids, which show more or less deviation owing to the fact that the methods used have been different or, at least, have not been sufficiently controlled. Yet, the agreement in the findings is sufficiently close to permit of certain general conclusions.

Balthazard and Lambert[1] showed that the presence of 2–3 grams of alcohol per liter of blood (0.2 to 0.3 per cent.) corresponded to nervous troubles in subjects unaccustomed to alcohol, while the presence of 3 grams per liter (0.3 per cent.) or over always corresponded to a condition of drunkenness, even in confirmed alcoholics. Schwarz[2] finds that 0.2 per cent. is associated with a light or average state of drunkenness, a concentration of 0.2 to 0.3 per cent. with a condition of average intoxication, while one of 0.3 per cent. or over is found in marked drunkenness, the highest figures in his cases showing 0.56 per cent. in the brain, 0.47 per cent. in the blood, and 0.42 per cent. in the urine. Schwarz refers to a case of Fischer in which 0.82 per cent. was found in the brain. Gettler and Tiber[3] find that the alcoholic content of the brain of persons taking alcohol ranges between 0.005 and 0.6 per cent., those having a content below 0.1 per cent. showing no abnormal physiologic effects, patients with an alcoholic content above 0.1 per cent. and up to 0.25 per cent. show some physiologic disturbance, but none of them presenting an unbalanced equilibrium, while those with an alcoholic content above 0.25 per cent. and up to 0.4 per cent. or as high as 0.6 per cent. manifest an unbalanced equilibrium, a condition commonly known as intoxication. Bogen[4] reports that none of his patients having less than 1 mg. of alcohol per cc. of urine (0.1 per cent.) was pronounced intoxicated, but more than half of those with from 1 to 2 mg., three-fourths of those with 3 mg., and almost every patient with 4 mg. or more were so diagnosed. Kionka[5] states that the amount of alcohol in the blood does not, necessarily, express the degree of intoxication, and that the concentration of alcohol in the urine never goes above 0.1014 per cent., but the experience of most workers is quite contrary to this finding. It is to be remembered, in this connection, that there may be cases of true intoxication in which the concentration of alcohol in the urine and blood may fall much lower than those stated above, as some individuals undoubtedly react with an abnormal condition of intoxication following ingestion of relatively small amounts of alcohol. For this reason, clinical evidence must be taken into consideration in such cases, instead of relying entirely upon the findings of the chemist.

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[1] Ann. de méd. légale, 1921, **1**, 83. See, also, Vielledent, Ibid., 1926, **6**, 214.

[2] Schweiz. med. Wchnschr., 1926, **56**, 923.

[3] Arch. Path. and Lab. Med., 1927, **3**, 218. See, also, Zangger, "Die Organische Gifte" in *Lehrbuch der Toxikologie* by Flury and Zangger, 1928, p. 185.

[4] Jour. Amer. Med. Assoc., 1927, **89**, 1508.

[5] Arch. f. exp. Path. u. Pharm., 1929, **128**, 133, 146 and 150.

From what precedes it seems probable that we have, in the examination of the blood, urine and cerebrospinal fluid, as well as the tissues, a means of determining rather closely the degree of intoxication. If the alcohol content runs from 0.2 to 0.5 per cent., a condition of drunkenness exists, the degree depending upon the absolute concentration, while from 0.6 to 0.7 per cent. may prove fatal, and from 0.7 to 1 per cent. will, almost invariably, cause death. Assuming that the concentration of alcohol is approximately the same in the different organs and fluids, it follows that, if the percentage of alcohol be multiplied by the weight of the individual, the product will represent, in a general way, the total quantity of alcohol taken[1].

Chronic Alcoholism.—A discussion of chronic alcoholism, like one of the opium or cocaine habit, does not properly fall within the scope of this book. A few remarks will be made, however, as there appears to be some variation in the type of chronic alcoholism existing at the present time from that formerly noted. The effects of long-continued use of alcohol have been of a general nature, characterized by a tendency to dilatation of the vessels, with such results as slight hemorrhages, acne rosacea, etc., gastritis with morning vomiting, symptoms of arteriosclerosis, hepatic cirrhosis, and weakness of the cardiac musculature, together with various disturbances of the nervous system, such as tremor, polyneuritis, and various psychoses. Especially to be mentioned is delirium tremens, characterized by disorientation as regards time and place, and by hallucinations of sight and hearing. It is an acute attack, frequently appearing without any warning, or being precipitated by a temporary excess of alcohol, by an accident, by an acute inflammation, etc. The hallucinations and illusions not infrequently lead the individual to commit homicide or suicide. It is interesting to note the variation in type of cases of chronic alcoholism seen at the present time, as contrasted with the prevailing symptomatology in pre-Volstead days. Thus Miller[2] reports the incidence of portal cirrhosis in Cook County Hospital from 1910 to 1920. For each year between 1910 and 1917 there were never fewer than 132 cases, and in one year the number ran as high as 160, while by 1919 the cases decreased to 48 and in 1920 there were only 19. Capps and Coleman[3] report that the cases of delirium tremens decreased in Cook County Hospital from 33 in 1916 to only 1 for the years 1921 and 1922 together, while Gerty[1] states that the diagnosis of chronic alcoholism with mental deterioration is made more commonly than ever before, this deterioration being either of a simple type rendering the individual unable to cope successfully with his environment, or of the delusional type, which makes him a menace when unconfined in an institution.

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[1] See McNally and Embree, Arch. Path., 1928, **5**, 607; and Naville, Revue Méd de la Suisse Rom., 1928, **48**, 849.

[2] Jour. Amer. Med. Assoc., 1921, **76**, 1646.

[3] Ibid., 1923, **80**, 750.

Fatal Dose.—The fatal dose of alcohol varies with the age of the individual, with his tolerance, and with his general health, as well as with the strength of the alcoholic taken. As previously stated, a concentration of 0.7 to 1 per cent. of alcohol in the blood and tissues will cause death. Such a concentration would, under ordinary circumstances, be furnished by the drinking of 1 to 2 pints of whisky or brandy, corresponding to 8 to 16 ounces of absolute alcohol, although it is probable that ½ of this quantity would prove fatal if taken in concentrated form at one time. A 6 months old child died from the effects of 2 tablespoonfuls of brandy, while 500 grams of brandy, as also, ¾ liter of cognac, have proven fatal to adults. Recovery has occurred from much larger quantities, both in children and in adults.

Fatal Period.—Death may occur in a few minutes, or be delayed for five or six days. In most cases, however, death is observed in from 5 to 10 hours after the comatose state begins, recovery being rare if the coma lasts longer than 10 to 12 hours after the drinking bout.

Treatment.—If vomiting has not freely occurred, wash out the stomach with warm water. The body temperature should be maintained by hot applications, and collapse symptoms treated by the administration of strong coffee, digitalis, strychnine, etc. According to Wullften-Palthe[2] inhalation of oxygen is valuable in arresting the intoxication by overcoming the tendency to anoxemia. The patient may be quieted by bromides or other hypnotics, morphine and scopolamine being used, preferably, when alcoholic mania is present. In deep coma, artificial respiration may be necessary, and warm baths followed by cold affusions are, often, useful.

Postmortem Appearances.—Cadaveric rigidity may last for a considerable period. The organs, especially the brain, may have a distinct odor of alcohol. As a rule the stomach and esophagus show more or less hyperemia, punctiform ecchymoses being, often, noted, and the mucous membrane being easily separated, although in some cases the appearances may be practically normal. Edema of the lungs is somewhat frequent, and cloudy swelling and early fatty degeneration of the liver is usual, Wallace[3] calling attention to the increase of bilirubin in the blood and urobilinogen in the urine as definite evidence of hepatic injury. The brain is edematous and hyperemic, and there may be a serous effusion into the ventricles. The kidneys may show a mild diffuse nephritis.

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[1] Ill. Med. Jour., 1924, **46**, 141.

[2] Deutsch. Ztschr. f. Nervenhkde., 1926, **92**, 79; Geneeskund. Tijdschr. Nederland. Indië, 1928, **68**, 597; Abs. in Chem. Abs., 1929, **23**, 1676.

[3] Proc. Soc. Exp. Biol. and Med., 1927, **24**, 598.

In the chronic types of alcohol poisoning, petechial hemorrhages in the gastric mucosa are quite constant, these probably being anatomic manifestations of an acute toxemia[1]. The stomach may show signs of chronic inflammation, although Hirsch believes that chronic alcoholism is of doubtful etiologic importance as a cause of chronic gastritis. The liver is, not infrequently, cirrhotic and fatty, the kidneys may show evidences of chronic nephritis, and the large vessels are atheromatous. The brain may be edematous and atrophied, distinct histologic changes occurring in the cells of the brain and cord[2].

Detection.—In the usual process of obtaining volatile poisons by distillation with steam, alcohol is found in the distillate, along with other substances, some of which may give reactions which may be confused with those of alcohol. The material under investigation is finely comminuted, placed in a large distilling flask, sufficient water is added to give a consistency of gruel, the mixture slightly acidified with tartaric acid, and the flask connected in the usual manner for distilling with steam. The tip of the condenser tube should be placed under a little distilled water in the receiving flask, in order to prevent loss of volatile substances. The distillation is carried out until about 1 cc. is obtained for each gram of tissue used for the determination. With this distillate the following qualitative tests may be carried out.

1. *Lieben's Iodoform Test.*—To a few cc. of the suspected distillate add a little aqueous solution of iodine in potassium iodide and enough 10 per cent. sodium hydroxide solution to change the color of the mixture from a brown to a distinct yellow. On slightly warming this mixture a distinct odor of iodoform will be obtained, and a yellow precipitate, appearing under the microscope as small hexagonal crystals, will be observed if alcohol be present. If the amount of alcohol be small, these crystals may not appear until the solution has cooled, or after long standing. This reaction is a very delicate one, but it is not characteristic of alcohol, as other primary alcohols (except methyl alcohol), many secondary alcohols, aldehydes, acetone, acetic ether (not ethyl ether), lactic acid, and other organic substances give this test. For this reason it is necessary to test the distillate for aldehydes and acetone, especially, before stating that alcohol is present. If either or both of these be present, it may be necessary to redistill the distillate, discarding about 10 per cent. of the distillate, which will contain practically all of the acetone. To the remaining distillate, add a little 10 per cent. sodium hydroxide and a few cc. of a 10 per cent. silver nitrate solution, in order to oxidize the aldehydes and saponify any of the fats present, and distill again. On now retesting the distillate, a positive iodoform reaction will indicate the presence of

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[1] Hirsch, Arch. Int. Med., 1916, **17**, 354.

[2] See Laignel-Lavastine, Bull. et mém. Soc. méd. des hôp. de Paris, 1920, **44**, 1432.

alcohol, as a rule, as practically none of the other substances giving a positive iodoform test will be present in the purified distillate.

2. *Berthelot's Test.*—Shake a few cc. of the suspected distillate with a drop or two of benzoyl chloride, and then add 10 per cent. sodium hydroxide solution to a strong alkaline reaction. On slight warming, the aromatic odor of ethyl benzoate will appear, and the irritating odor of benzoyl chloride disappears, if alcohol be present.

3. *Ethyl Acetate Test.*—To the suspected distillate add an equal volume of concentrated sulphuric acid and then some solid sodium acetate. On warming the mixture, the pleasant odor of ethyl acetate appears in the presence of alcohol.

4. *Chromic Acid Test.*—Mix the suspected distillate with dilute sulphuric acid, and add a few drops of dilute potassium bichromate solution. On warming the mixture the odor of acetaldehyde will be recognized, and the color of the mixture will change from red to green, if alcohol be present. This test is not characteristic of alcohol, as other volatile substances may, also, give the test.

5. *Vitali's Test.*—Mix a little of the suspected distillate with a little solid potassium hydroxide and a few drops of carbon disulphide. Allow to stand until the odor of carbon disulphide is dispelled, add a drop of 10 per cent. ammonium molybdate solution, and acidify with dilute sulphuric acid. In the presence of alcohol a wine-red color will be produced.

6. *Taylor-Bucheim's Test.*—This test depends upon the oxidation of the alcohol to acetaldehyde and acetic acid, and is best made with the original tissue. Place some of the finely comminuted tissue, or a little blood or urine, in a small flask, add a little water, and test the fluid for neutrality, neutralizing if necessary. To the flask attach a right-angled tube which contains a layer of platinum black, and a little distance beyond this catalyzing substance place a few strips of blue litmus paper. Now heat the flask on the water-bath. The vapors passing through the platinum black will, if alcohol be present, be converted into those of acetaldehyde and acetic acid, the former being recognized by its odor and the latter by changing the color of the strips of litmus to red.

Quantitative Estimation.—In any toxicologic investigation it is necessary to determine the quantity of alcohol present in the tissues, if one is to be in a position to give any conclusion as to the existence of an alcoholic poisoning. In police investigations it, often, becomes necessary to determine whether or not a person is drunk, and this is, not infrequently, possible if the blood or urine be examined quantitatively, even when there has been little chance of observing the individual clinically.

Many different methods have been advocated for such determinations, some of these depending upon the titration of the alcohol by a standard solution of potassium bichromate in sulphuric acid solution, others based on the oxidation of the alcohol to acetic acid and the titration of this latter substance, still others using the oxidation of alcohol to acetaldehyde and the estimation of this oxidation product colorimetrically with fuchsin-sulphurous acid, some others employing the formation of iodine or other derivatives of alcohol and the estimation of such compounds, and quite a number using such physical methods as the coefficient of expansion, electric conductivity, cryoscopy, specific gravity, and refractometry. It should be said that all of these methods have some faults, positive or negative errors creeping in in spite of all precautions taken. There is practically no examination in forensic chemistry that is 100 per cent. accurate, as there is, necessarily, some loss of material in the various analytic steps, so that we must content ourselves, in the selection of methods for determining alcohol, with approximate estimations, admitting that the yield of oxidation or other products may not be absolutely quantitative.

The Nicloux Method[1].—This method has, probably, been more widely used and more often modified than any other one for estimation of alcohol[2]. The method depends upon the fact that, when a solution of alcohol is treated with potassium bichromate in the presence of sulphuric acid, the alcohol is oxidized, under the conditions of the test, largely to acetaldehyde, while the bichromate is reduced with the formation of chromic sulphate, according to the equation,

$$3C_2H_5OH + 4H_2SO_4 + K_2Cr_2O_7 = 3CH_3CHO + Cr_2(SO_4)_3 + K_2SO_4 + 7H_2O.$$

If a standard solution of potassium bichromate be used, the calculation of the alcohol present is a simple process.

A weighed amount (usually 100 grams) of the finely comminuted tissue, or a measured volume of blood or urine (10 cc. will suffice), should be placed in a distilling flask, mixed with a little water, acidified with tartaric acid, and distilled with steam in the usual manner. Special apparatus may be devised for this purpose, but, if all connections are tight, little chance of loss of volatile material need be feared, especially if the condenser be well cooled and the receiving flask be kept cool with ice water. The distillation is continued until about 1 cc. is obtained for each gram of tissue or each cc. of fluid used. If acetone or aldehydes have been found in the qualitative tests of the distillate, redistillation should be carried out after treating the first distillate with about 5 cc. of 10 per cent. sodium hydroxide and 3 cc. of 10 per cent. silver nitrate solution. The distillate, which must be, of course, carefully measured, is then treated as follows[3]: By means of an accurately calibrated pipet, place 5 cc. of the well-mixed distillate in a small (30 cc.) Erlenmeyer flask, add from a buret 3 cc. of concentrated sulphuric acid, and titrate with a standard solution of potassium bichromate containing 19 grams to the liter[4], using a buret graduated to 0.05 cc. Add the bichromate a few drops at a time, shaking after each addition, until the blue-green color first appearing is changed to a yellow green[1]. Now place the flask in water at 100°C. for 2 minutes, and add more bichromate if the yellow-green color does not persist after the heating. Read off the amount of bichromate solution used to produce the change in color, and check this result by a duplicate determination with another 5 cc. of the distillate, using at once slightly less than the total amount of bichromate employed in the first titration, and finishing the titration by careful addition of more bichromate. 1 cc. of bichromate used corresponds to 0.005 cc. of absolute alcohol, hence it follows that 1 cc. of the bichromate is equivalent to 0.1 per cent. (in terms of cc.) of alcohol in the distillate, as 5 cc. were used in the titration. If the figure obtained by titration be multipled by the volume of distillate, the result is the amount of alcohol in cc. in the amount of tissue or fluid distilled. By simply multiplying this figure by the weight of the organ (if this be known), the total quantity may be determined.

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[1] Thése de Paris, 1900. For other papers of Nicloux see references on page 733.

[2] For bibliography of these modifications see Gettler and Tiber, Arch. Path. and Lab. Med.; 1927, **3**, 75; and Schwarz, Deutsch. Ztschr. f. d. g. ger. Med., 1927, **10**, 377.

[3] See McNally, Embree and Rust, Jour. Biol. Chem., 1927, **74**, 219.

[4] Schwarz, Deutsch. Ztschr. f. d. g. ger. Med., 1927, **10**, 377, employs a solution containing 16.97 grams of bichromate per liter.

While this method is open to the objections that the oxidation of the alcohol may not, always, stop at acetaldehyde and that acetic acid and even carbon dioxide may be formed, yet, if the conditions are kept as outlined above, the results will be quite constant, the danger of loss of acetaldehyde being only slight. Further, if precautions are taken to remove, as mentioned above, other volatile substances which might reduce the bichromate, the positive errors will be eliminated. If one works with this method until he is able to recognize the point at which the color change occurs, he will overcome the chief objection raised against the method, and will obtain check results with little trouble.

Method of Gettler and Tiber[2].—This method was developed by Gettler and Tiber in their work on the alcoholic content of brain tissue as they found from their investigations "that the alcoholic content of the brain gives the best and most consistent indication of the degree to which the alcohol had influenced the subject in question". The method is, however, applicable to any other tissue, but the factor subtracted for correction must be determined for these other tissues, although it is probable that the correction might be dispensed with, as the error involved is relatively slight.

The tissue (brain), as soon as it is removed from the body, should be placed in a tightly closed jar and put in a refrigerator. When it becomes ice cold, 500 grams are weighed out, quickly ground up and placed in a 2 liter flask. To this are added 600 cc. of water, 5 cc. of a saturated solution of tartaric acid, and 1 cc. of mineral oil. This mixture is then distilled with steam in the usual manner, a long, well cooled condenser being used and the distillation continued until exactly 800 cc. have been collected, in order to insure the distillation of all alcohol present. Place 20 grams of potassium bichromate and 40 cc. of concentrated sulphuric acid in a 500 cc. distilling flask, add 300 cc. of the well-mixed distillate, and mix the contents well. Connect the flask to a long well cooled condenser by means of a Hopkins distilling head, and distill, regulating the heat so that it requires from 45 to 50 minutes to collect exactliy 250 cc. of distillate. Thoroughly mix the distillate, place 50 cc. of ths in an Erlenmeyer flask, and titrate with N/20 sodium hydroxide solution, using phenolphthalein as an indicator. The number of cc. of sodium hydroxide used is read off, and from this should be subtracted 1.32 cc., which represents the correction for the volatile acid-reacting material obtained from the same amount of distillate from normal brains. One cc. of N/20 sodium hydroxide is equivalent to 2.3 mg. of ethyl alcohol, hence by multiplying this factor by the number of corrected cc. of sodium hydroxide used, we obtain the amount of alcohol in mg. per 50 cc. of the second distillate, and by multiplying this figure by 5 we get the total alcohol recovered from the total 250cc. of second distillate, which represents 300 cc. of the original distillate. As 800 cc. of original distillate were collected, it follows that the amount of alcohol in the 500 grams of brain tissue subjected to distillation will be $2\frac{2}{3}$ times the figure obtained from the 300 cc. of original distillate. Gettler and Tiber have found that the average yield of acetic acid recovered by this method is 85.67 per cent., hence, to obtain the actual amount of alcohol present in the 500 grams of brain tissue, one must multiply the figure obtained by the calculation mentioned in the last sentence by 1.167. To simplify this calculation, Gettler and Tiber give the following formula: (CC. of N/20 sodium hydroxide used in the titration -1.32) $=$ mg. of alcohol per kilogram of tissue. If one wishes to express these figures in terms of volume, the figures by weight may be divided by 0.79357 (the specific gravity of absolute alcohol), or, what amounts to the same thing, multiplied by 1.26 the reciprocal of the specific gravity.

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[1] This color change is not the easiest one to determine accurately, so that the worker should work with a known amount of alcohol until he has become familiar with the changes in color. In this way he will protect himself from adding too much bichromate. The best results are obtained when the distillate requires between 0.5 and 1 cc. of bichromate.

[2] Arch. Path. and Lab. Med., 1927, **3**, 75 and 218.

Higher Alcohols

As previously stated the toxicity of the alcohols increases with the molecular weight, methyl alcohol being, however, an exception. The primary alcohols appear to be more harmful than the secondary[1], while the secondary are less toxic than the tertiary as a rule. These higher alcohols have much the same general action as ethyl alcohol, although their decreasing volatility tends to hold them in the system for a much longer period than the lower alcohols are retained. These higher alcohols are, largely, of toxicologic interest as impurities in preparations of ethyl alcohol, although some of them find usage in industries, and may lead to poisoning. Swenarton[2] has shown that the crude fusel oil from the industrial fermentation of molasses contains in addition to n-propyl, iso-butyl, secondary butyl carbinol and iso-butyl carbinol, alcohols of the hexylic, heptylic, octylic, nonylic, and decylic series.

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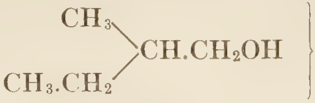
[1] See Macht, Jour. Pharm. and Exp. Therap., 1920, **16**, 1.

[2] Science, 1929, **70**, 554.

In his work on the development of eggs of sea urchins, Fühner[1] showed that propyl alcohol was 3 times as toxic as ethyl alcohol, and that normal butyl alcohol was, in its turn, 3 times more poisonous than propyl alcohol, a finding which has been repeatedly confirmed with warm-blooded animals. These alcohols, however, do not ordinarily concern us in toxicological work except in so far as they are constituents of "fusel oil", which is found in most of our stronger alcoholics. Both of these alcohols show the same general effects as ethyl alcohol, although much more marked in character. Substitution of chlorine for some of the hydrogens of such alcohols leads to the formation of products, which have marked sedative and hypnotic effects. Thus, chloretone (trichlor-tertiary butyl alcohol) is rather widely used, especially in animal experiments, for this purpose[2].

Iso-amyl Alcohol $(CH_3)_2:CH.CH_2.CH_2OH$) is the chief constituent of fusel oil, while an isomer (active amyl alcohol, methyl-ethyl-carbinol,  $\begin{matrix}CH_3\\ CH_3.CH_2\end{matrix}\!\!>CH.CH_2OH$) is the optically active constituent of the fusel oil. Fusel oil is used as a solvent for paints and is somewhat extensively employed in chemical industry and in routine organic laboratory work. Judging from the results of animal experiments, it is about 5 times as toxic as ethyl alcohol. It is this constituent that gives to brandy and whisky their unpleasant odor, although it is probable that the amount of fusel oil in these products is too small to warrant a conclusion that it plays a large rôle in the toxicity of alcoholic beverages. · The vapors of iso-amyl alcohol are irritating to the mucous membranes and are very unpleasant, inhalation, not infrequently, causing headache, palpitation of the heart, dyspnea, and coughing. Following large doses severe intoxication may arise, characterized by profound unconsciousness, suspension of respiration, and cyanosis[3]. It is difficult to give an idea as to the toxic dose of iso-amyl alcohol, as the literature is meager on this point. However, doses as small as 0.5 gram may produce headache, dyspnea, and coughing. Its toxic action is increased by the presence of ethyl alcohol, as it is then absorbed more readily, so that it is probable, as stated by Autenrieth[4], that a content of 0.3 per cent. of amyl alcohol in ethyl alcohol should be regarded as inadmissable.

Properties.—Iso-amyl alcohol is a thin, oily fluid with a penetrating and disagreeable odor and a burning taste. Its specific gravity is 0.818

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[1] Arch. f. exp. Path. und Pharm., 1905, **52**, 69.

[2] See Aldrich, Jour. Biol. Chem., 1918, **34**, 263, and Jour. Lab. and Clin. Med., 1919, **4**, 425, for a method of detecting this substance in tissues and body fluids.

[3] See Futcher, Amer. Med., 1901, **2**, 210, for report of 2 cases of poisoning.

[4] *Detection of Poisons*, 6th Amer. Ed., 1928, p. 78.

at 15.56°C., while its boiling point is 131°C. It is very sparingly soluble in water, but mixes in all proportions which alcohol, ether, chloroform, petroleum benzin, and benzene.

Detection.—Fusel oil may be obtained from the tissues by distillation with steam in the usual manner. If fusel oil is present, the distillate will, as a rule, be cloudy and may give the characteristic odor of iso-amyl alcohol. This distillate may, then, be shaken out with chloroform or ether, and the solvent allowed to evaporate spontaneously. Fusel oil will remain behind in the form of oily drops, which may be tested for their odor and the following chemical tests applied.

Marquardt's Test.—Place a drop or two of the suspected residue in a test-tube, add a little water and a few drops of dilute sulphuric acid, and, then, a few drops of potassium permanganate solution (1:1000) until a red color persists. Stopper the tube and allow to stand for 24 hours. Should the red color of the mixture disappear, add more permanganate solution from time to time, as may be required. On testing the odor of the mixture from time to time, there will appear in succession the odor of valerianic aldehyde, the amyl ester of valerianic acid, and, finally, that of valerianic acid.

Uffelmann's Test.—To a few drops of the suspected residue add four times its volume of a freshly prepared methyl violet solution which has been colored green by the addition of hydrochloric acid[1]. If fusel oil is present reddish violet drops appear at once on the green fluid. This test may prove valuable when the material under investigation contains substances, other than fusel oil, which have strong odors, which might interfere with the recognition by Marquardt's test, although valerianic acid has a very distinctive odor.

The estimation of the quantity of fusel oil is rarely of significance except in examination of alcoholic beverages. For this reason we shall refer to other works for such quantitative determinations[2].

Tertiary Amyl Alcohol (dimethyl ethyl carbinol, $(CH_3)_2{:}COH.CH_2.CH_3$) is known in medicine as amylene hydrate, and has been somewhat used as an hypnotic. Its action is characterized by profound narcosis, unconsciousness occasionally lasting for 2 or 3 days, and by marked disturbance of circulation and respiration. A few cases of poisoning have been reported and, at least, 1 fatal case[3], following rectal administration of 35 grams.

This amyl alcohol is a colorless liquid with an odor resembling both camphor and peppermint. It has a specific gravity of 0.814 and a boiling point of 102.5°C. On oxidation, as in Marquardt's test, it yields acetone, acetic acid and carbon dioxide.

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[1] This is prepared by adding to a mixture of 1 part of methyl violet and 100 parts of water enough 0.2 per cent. HCl to color the solution green.

[2] See "Non-alkaloidal Organic Poisons" by Hunt and Gettler, in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 624. Also, *Official and Tentative Methods of Analysis of the Association of Official Agricultural Chemists*, 2nd ed. 1925, p. 371.

[3] Jacobi and Speer, Therap. Halbmonatshft., 1920, **34**, 495.

ALDEHYDES

In the group of aliphatic aldehydes, the most important members from the toxicologic standpoint are formaldehyde and acetaldehyde, both of which are used in industry and in medical practice and have lead to severe and fatal poisoning in some cases. Such chlorine derivatives as chloral must, however, receive attention in this connection.

FORMALDEHYDE

Formaldehyde finds rather extensive use in chemical industry in the preparation of organic dyes, as well as in tanning and photographic processes. It is a valuable disinfectant, deodorizing agent, and preservative, having been used somewhat widely in preserving milk and other articles of food, but now being generally prohibited by the law in the United States.

Probably the first case of fatal poisoning with formaldehyde was reported by Bock[1] in 1899. According to Kline[2], there are recorded in the literature only 27 cases of formaldehyde poisoning, twelve of which were fatal. Of these twelve, seven were males, who had mistaken the solution of formaldehyde for whisky or water, and five were females, who had taken the solution with suicidal intent.

Properties.—Formaldehyde ($HCHO$) is a colorless, irritating gas, prepared by the oxidation of methyl alcohol. At $-20°C.$ it condenses into a colorless liquid, and solidifies at $-90°C.$, while at temperatures of 20°C. and above it polymerizes to paraformaldehyde (trioxymethylene $(HCHO)_3$). It is freely soluble in water, the official Liquor Formaldehydi (commonly known as "formalin") being an aqueous solution containing not less than 37 per cent. of formaldehyde with variable amounts of ethyl or methyl alcohol, or both, to prevent polymerization. The official Paraformaldehydum (paraform) occurs in white, friable masses, or as a white powder, having a slight odor of formaldehyde. It is very slowly soluble in cold water, more readily soluble in hot water with the formation of formaldehyde; insoluble in alcohol and in ether; but readily soluble in solutions of fixed alkali hydroxides. On heating formaldehyde with dilute caustic alkali, it splits into methyl alcohol and a formate, an action which probably occurs when the vapors come in contact with the proteins of the surface cells of the mucous membranes; while on standing with ammonia it yields methenamine (hexamethylenetetramine, urotropin, $(CH_2)_6N_4$).

Symptoms.—The vapor of formaldehyde is very irritating to the mucous membranes with which it comes in contact, causing stinging and prickling in the nose and throat, salivation, conjunctival and bronchial irritation. Workmen subjected to such fumes suffer quite severely from coryza, conjunctivitis, and bronchitis. The special feature of the action following inhalation of the vapors is irritation and inflammation of the respiratory tract.

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[1] Fort Wayne Med. Jour., 1899, **19**, 249.

[2] Arch. Int. Med., 1925, **36**, 220.

Weak solutions of formaldehyde are very irritating to the skin, producing an eczematous condition, while long continued application of strong solutions may lead to ulceration and gangrene. Individuals differ markedly in susceptibility to this skin irritation, but, after a skin has once been severely irritated, it may become very sensitive to the later action of formaldehyde.

When solutions of formaldehyde are swallowed the symptoms noted are a mixture of those of local irritation with slight general systemic effects. Formaldehyde is somewhat rapidly absorbed from the alimentary tract, as well as from the lungs, although it is probable that the amount absorbed from the respiratory tract plays a small role in the systemic effects. The chief symptoms noted are burning in the throat and esophagus, intense epigastric pain, usually vomiting of blood-tinged material, and occasionally diarrhea. In some cases the irritation in the throat is so marked that the patient is unable to speak[1], while the respiratory irritation may lead to a bronchitis with a hoarse laryngeal cough, the blood showing an eosinophilia[2]. The systemic effects appear to be exerted upon the central nervous system, Brunnthaler[3] believing that even inhalation of formaldehyde may cause a cumulative action analogous to that of methyl alcohol. The general symptoms are vertigo, stupor, unconsciousness, convulsions, coma, and death.

Fatal Dose.—The average fatal dose of formalin appears to be about 3 ounces[4], although "a few drops" have proven fatal to a boy of 3 years[5], while 1 ounce has caused death of adults in at least 2 cases[6]. On the other hand, recovery has followed the taking of various quantities up to 4 ounces (120 cc.)[7], which appears to be the largest dose from which recovery followed.

Fatal Period.—In the reported cases death has occurred at varying periods ranging from 20 to 30 minutes[8] to 4 weeks[9], while some cases die in a few hours[10] and others linger for several days.

Treatment.—The stomach should be washed out promptly to remove the formaldehyde, dilute ammonia or ammonium acetate solution being added to the wash water to neutralize the formaldehyde by the formation of methenamine. In some cases the stomach tube can not be passed owing to the esophageal constriction which may be present. In such cases apomorphine may be given to induce emesis. For the systemic effects, the treatment should be symptomatic, but little is to be expected from such treatment if the irritant effects are extreme.

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[1] See MacLachlan, Cleveland Med. Jour., 1909, **8,** 606.

[2] Trenkel, Inaug. Dissert., Munich, 1917.

[3] Zentralbl. f. Gewerbehyg., 1914, **2,** 24. See, also, Kluber, Münch. med. Wchnschr., 1900, **47,** 1416.

[4] See Kline. Arch. Int. Med., 1925, **36,** 220 for a review of recorded cases.

[5] Ely, Jour. Amer. Med. Assoc., 1910, **54,** 1140.

[6] Watt, Brit. Med. Jour., 1912, **2,** 350; and Shaposhnikoff, Terap. Obozr., 1912, **5,** 537.

[7] Hale, Jour. Amer. Med. Assoc., 1922, **78,** 452.

[8] Levison, Ibid., 1904, **42,** 1492; and DeRechter, Arch. Int. de Méd. Légale, 1914, **5,** 44.

[9] Moorhead, Brit. Med. Jour., 1912, **2,** 1470.

[10] Watt, Ibid., 1912, **2,** 350; and Kline, Arch. Int. Med., 1925, **36,** 220.

Postmortem Appearances.—A summary of the pathologic changes found in formaldehyde poisoning in 10 of the 12 fatal cases reported is given by Kline[1] as follows: "In all these, the changes were most marked in the lower esophagus and to an even greater extent in the stomach. The changes in these organs varied from simple hardening of the tissues to extreme corrosion. Frequently, marked congestion and edema were present with areas of erosion and of hemorrhage. Occasionally similar but less marked changes were observed in the duodenum and even jejunum. The remainder of the alimentary canal rarely showed any abnormality. In cases continuing thirteen hours or longer after ingestion of the formaldehyde, degenerative changes in the parenchymatous organs were noted, varying from slight cloudy swelling to fatty degeneration and even patchy necrosis. In a few cases the blood was still fluid and was dark red at the time of the necropsy. . . . In one case death was apparently due to diffuse bronchopneumonia. In a few others, there was a terminal pulmonary edema."

Detection.—In cases of formaldehyde poisoning, the poison is found especially in the stomach and contents and in the intestines, although the other organs will yield their quota. The usual method of distillation of the acidified material with steam effects the isolation of formaldehyde. Although formaldehyde comes over, in ordinary distillations of fluid materials, in the first 20 to 25 cc. of the distillate, yet it may happen that it may distill very slowly, even in the presence of a rapid current of steam. Autenrieth[2] states that it may distill over very slowly from parts of a cadaver, in one case it being necessary for him to use a paraffin bath, to replace the water frequently, and to carry the distillation nearly to dryness before even a faint trace of formaldehyde was obtained. Smith[3] shows that the first 20 cc. of distillate, or $\frac{1}{5}$ the original volume, contain practically $\frac{1}{3}$ of the total formaldehyde. To this distillate the following tests may be applied.

Fuchsin-sulphurous Acid Test.—To 2 cc. of the distillate add 1 cc. of concentrated sulphuric acid and cool. To this mixture add 5 cc. of the fuchsin-sulphurous acid reagent[4], mix thoroughly, and allow to stand for a few minutes. In the presence of formaldehyde a violet-red or blue color develops within 10 minutes and may become more intense on longer standing.

Morphine-sulphuric Acid Test.—To 3 cc. of distillate add 5 cc. of concentrated sulphuric acid, mix, and cool. On adding to this mixture a trace of morphine, a purple-red color, changing to blue-violet, and finally to pure indigo blue will indicate the presence of formaldehyde.

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[1] Arch. Int. Med., 1925, **36**, 220.

[2] *Detection of Poisons*, 6th Amer. Ed., 1928, p. 79.

[3] Jour. Amer. Chem. Soc., 1903, **25**, 1032 and 1037.

[4] Schiff-Elvove reagent, prepared by method given on page 727.

Acetaldehyde gives with this test only yellow colors. This test is especially sensitive and characteristic.

Hehner's Test.—To 3 cc. of distillate, add 3 cc. of fresh unboiled milk and 5 cc. of concentrated hydrochloric (or sulphuric) acid containing a trace of ferric chloride (for each 100 cc. about 0.2 cc. of 10 per cent. ferric chloride solution). Place this mixture in a boiling water bath for a few minutes. In the presence of formaldehyde a violet color appears. This test is very delicate, but its sensitiveness is strongly influenced by the presence of acetaldehyde.

Phenylhydrazine Test.—To 2 cc. of the distillate add 10 drops of a 5 per cent. aqueous solution of phenylhydrazine hydrochloride, 1 or 2 drops of a 0.5 per cent. solution of sodium nitroprusside, and 10 drops of 10 per cent. sodium hydroxide solution. If formaldehyde is present, a blue color develops, which changes to green and then to yellowish red. With this test acetaldehyde gives a red color.

Phlorogucinol Test.—To 2 cc. of the distillate add 1 or 2 drops of a 1 per cent. alcoholic solution of phlorogucinol and sufficient luke-warm sodium hydroxide solution to make the mixture about N/10 alkaline and warm slightly. In the presence of formaldehyde a red color is produced.

Methenamine Test.—To 10 cc. of the distillate in an evaporating dish add 10 cc. of concentrated ammonia water and evaporate just to dryness on the water-bath. The formaldehyde condenses with the ammonia to form methenamine. Dissolve the residue in a few drops of water, and add a drop of mercuric chloride solution, when characteristic crystals of methenamine-mercuric chloride form, the shape of the crystals varying with the concentration.

Estimation.—While the quantitative estimation of formaldehyde is of only slight importance in forensic analysis, yet it is, not infrequently, necessary to know how much of this poison may be present in the tissues. Many methods have been advocated for such estimation, but few, if any, of them yield absolutely accurate quantitative figures with tissue distillates. For general purposes we prefer the method of Romijn,[1] which depends upon the fact that formaldehyde is oxidized by iodine in alkaline solution to formic acid. By back-titration of the iodine remaining uncombined after the reaction, one may determine the amount of iodine used and, as a consequence, the amount of formaldehyde present, 2 atoms of iodine being the equivalent of 1 molecule of formaldehyde. In this method, however, no substances, such as other aldehydes, alcohol, acetone, etc., should be present, as these will combine with iodine and introduce erroneous results. Further, it is assumed, as shown by Smith,[2] that the first 20 cc. of the distillate from the organs, contains ⅓ the total formaldehyde present.

To 100 grams of the finely comminuted tissue add a little sulphuric or phosphoric acid and distill with steam, collecting exactly 20 cc. of distillate. To 10 cc. of the distillate in a glass-stoppered flask add 25 cc. of N/10 iodine solution and, then, drop by drop sufficient sodium hydroxide solution to produce a light yellow color. Stopper the flask, shake the mixture, and allow to stand for 10 minutes protected from the light. Now acidify the mixture with hydrochloric acid to set free the uncombined iodine, and titrate the liberated iodine with N/10 sodium thiosulphate solution, using starch solution as indicator. Subtract the number of cc. of sodium thiosulphate used in this titration from 25 (the cc. of N/10 iodine solution originally added) to obtain the number of cc. of N/10 iodine used in the oxidation process. 1 cc. of N/10 iodine equals 1.5 mg. formaldehyde. Multiply this factor by the number of cc. of iodine used, and, in turn, multiply this latter figure by 2 to obtain the formaldehyde in the 20 cc. of original distillate. By multiplying this last figure by 3, we obtain the amount of formaldehyde in 100 grams of tissue.

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[1] Ztschr. f. anal. Chem., 1897, **36**, 18.

[2] Jour. Amer. Chem. Soc., 1903, **25**, 1032 and 1037.

ACETALDEHYDE

Acetaldehyde (ethyl aldehyde, ethylidene oxide, ethanal, CH_3CHO) is found in the first runnings in the rectification of spirits, and is formed, also, by the oxidation of alcohol when filtered through charcoal. It finds some use in the arts, but, per se, is not employed in medicine. It is a colorless, mobile, irritating liquid with a peculiar odor. Its specific gravity is 0.8009 and its boiling point 20.8°C. It is miscible in all proportions with water, alcohol, and ether. It oxidizes somewhat readily to acetic acid.

Inhalation of vapors of acetaldehyde may produce bronchial irritation with dyspnea and cough, while it may act somewhat like alcohol in producing intoxication and even anesthesia. It produces corrosion of the tissues, similar to formaldehyde, and hemolyzes the red cells with the production of methemoglobin. According to Iwanow it is more toxic than formaldehyde, 20 mg. per liter of air proving fatal in 1 to 2 hours.

PARALDEHYDE

On adding a few drops of sulphuric acid at ordinary temperatures, acetaldehyde is polymerized into paraldehyde, $(CH_3CHO)_3$, while at temperatures below zero metaldehyde is formed, the former being a liquid while the latter is a solid subliming at 112°C.

Paraldehyde has been used somewhat widely as a soporific and possesses some advantages over members of the chloral group as it does not seem to depress the heart to any extent. Acute fatal poisoning from paraldehyde is rare, although a few cases are reported, while chronic poisoning seems to be more common, owing to the fact that some individuals use it much as other employ alcohol, morphine, etc.

Properties.—Paraldehyde is official and appears in the form of a colorless, transparent liquid, with a strong, characteristic, not unpleasant or pungent odor, but with a burning, disagreeable taste. It is soluble in 8 parts of water at 25°C., but is less soluble in boiling water (1 in 17 parts). It is miscible with alcohol, ether, chloroform, and volatile oils. Its specific gravity at 25°C. is about 0.990, and it boils at 124°C. Heated with a little sulphuric acid, it is converted into acetaldehyde.

Symptoms.—Paraldehyde resembles alcohol to some extent in its action, although it is a much more powerful hypnotic and rarely causes any excitement. Its action is quite rapid, unconsciousness appearing promptly and lasting several hours, little cardiac or respiratory distress being observed. Large doses may cause nausea, vomiting, headache, and dizziness, while the period of unconsciousness may continue for 24 hours or more[1]. It is excreted partly by the lungs, but chiefly in the urine, but the disagreeable odor may remain in the breath for some time after the subject awakens.

The symptoms of chronic paraldehyde poisoning resemble, in some cases, those of chronic alcoholism, a condition somewhat similar to delirium tremens being noted[2], while other cases may show a state not unlike that seen under morphine[3]. Usually disturbances of digestion, thirst, emaciation, general muscular weakness, mental failure, with tremors of the hands and tongue are noted. In some cases there may be considerable mental confusion, hallucinations, and delusions[4].

Fatal Dose and Period.—The fatal dose of paraldehyde is difficult to state, as very large quantities have been taken without any serious consequences, other than prolonged unconsciousness. In one case[5] approximately 25 cc. caused unconsciousness in 5 minutes and death in 4 hours, while in another case[6] 3½ ounces caused severe, but not fatal, poisoning. Those accustomed to paraldehyde rapidly establish a tolerance, so that large doses (such as 16 to 18 ounces per day) may be taken with slight effects.

Treatment.—Gastric lavage should be carried out promptly. Stimulants, such as strychnine, hot coffee, and digitalis may be employed. The body temperature should be maintained by hot applications. Artificial respiration may be called for.

Postmortem Appearances. Nothing characteristic is found at autopsy. There may be signs of gastric irritation[7], while the stomach contents may smell strong of paraldehyde.

Detection.—Acetaldehyde is isolated from the tissues by the usual process of distillation with steam. Likewise, paraldehyde and metaldehyde, when heated wih acid, will pass over in the distillate as acetaldehyde. It follows, therefore, that if the distillate be tested for acetaldehyde, one will be unable to state definitely whether acetaldehyde or paraldehyde was originally present. In some cases it is possible to differentiate these aldehydes by detecting the strong, characteristic odor of paraldehyde. Acetaldehyde will give the iodoform reaction, as discussed under ethyl alcohol, while paraldehyde will not show this reaction until distilled with dilute acid, so that differentiation may be possible by testing the original extract by the iodoform test. There are certain general aldehyde reactions, such as the formation of a silver mirror by warming an ammoniacal silver nitrate solution in the presence of an aldehyde, the production of a yellow to yellowish-red precipitate with Nessler's solution, and the formation of a coloration with fuchsin-sulphurous acid, which serve to classify the substance as an aldehyde. If aldehydes have been shown to be present, one may employ the Morphine-Sulphuric Acid and the Phenylhydrazine tests, as outlined on pages 748 and 749, when the colors produced will show whether formaldehyde or acetaldehyde is present. Acetaldehyde vapors, on passing over platinum black, are converted into those of acetic acid, while the vapor of formaldehyde yields formic acid.

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[1] MacKenzie, Brit. Med. Jour., 1891, **2**, 1254, reports a case of stupor for 34 hours.

[2] Fornaca and Quarelli, Berl. klin. Wchnschr., 1912, **49**, 2451.

[3] Hartz, Jour. Amer. Med. Assoc., 1912, **58**, 625.

[4] Elkins, Quarterly Jour. of Inebriety, 1894, **16**, 333.

[5] O'Brien Case, Lancet, 1890, **2**, 423.

[6] MacKenzie, Brit. Med. Jour., 1891, **2**, 1254.

[7] See Paltauf, Wien. klin. Wchnschr., 1893, **6**, 888. Also, Schneider, Ibid., 1929, **42**, 357; Bau, Deutsch. Ztschr. f. d. ges. ger. Med., 1929, **13**, 337.

CHLORAL HYDRATE

Chloral hydrate has been somewhat widely used as an hypnotic, but of recent years it has fallen into disrepute, owing to its dangerous action upon the heart. Most of the cases of poisoning from chloral hydrate have been accidental, due to medicinal overdoses or to mistakes in taking the drug. Some cases have, also, been reported from the use of proprietary preparations, such as bromidia[1], which contains about 12 grains of chloral hydrate per fluidram. Witthaus[2] has collated the reports of 136 cases of poisoning by chloral hydrate, of which 104 were accidental, 28 suicidal, and 4 criminal. Of the suicidal cases only 9 of the 28 cases were successful, while the criminal cases have been associated with the administration of the drug for purposes of robbery or rape, rather than with deliberate intent to cause death, the chloral hydrate being used, largely, in the form of the so-called "knock-out drops". Although the drug has been usually taken by mouth, in these cases of poisoning, death has occurred from its introduction into the rectum and from intravenous injection.

Properties.—Chloral (trichlor-acetaldehyde, CCl_3CHO) is an oily, pungent smelling liquid, with a boiling point of 97°C. It gives the reactions of aldehydes, and is oxidized to trichloracetic acid. Pure chloral is not used as a therapeutic agent, but its hydrate, Chloral Hydrate (*Chloralis Hydras*, trichlorethylidene glycol, $CCl_3CH(OH)_2$) is official. This hydrate occurs in the form of colorless, transparent crystals, having an aromatic, penetrating, and slightly acrid odor, and a slightly bitter, caustic taste, which is almost lost when the hydrate is in solution in alcoholic beverages. It is slowly volatilized on exposure to air, melts at 57°C. and boils at 96° to 98°C. One gram of chloral hydrate is soluble in 0.25 cc. of water, 1.3 cc. of alcohol, 2 cc. of chloroform, and in 1.5 cc. of ether at 25°C. It is very soluble in olive oil and freely soluble in oil of turpentine. It is readily decomposed by caustic alkalies, alkali earths, and ammonia into chloroform, a formate of the base used, and water, but the alkalinity of the blood is not sufficient to bring this about.

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[1] See Report of Council of Pharmacy and Chemistry, Jour. Amer. Med. Assoc., 1914, **62**, 1573; Wood, Ibid., 1906, **46**, 1220; and Bennett, Ibid., 1922, **79**, 1048.

[2] *Toxicology*, 1911, p. 1177. See, also, Kane, Medical Record, 1880, **18**, 702; 1881, **19**, 4, 32, 60, 284, 310, 460, and 482.

Symptoms.—The action of chloral hydrate is much the same as that of alcohol or chloroform, although the effects sought therapeutically are slighter and more lasting than those of the anesthetics. The absorption of chloral hydrate from the bowel is relatively rapid, so that the effects come on within a few minutes, as a rule. The excretion is largely by the urine, in the form of urochloralic acid, a conjugated glycuronic acid.

With small doses of chloral hydrate, drowsiness and weariness appear, these symptoms passing, usually, into a state resembling natural sleep, from which the subject may be awakened by ordinary means. This sleep ordinarily passes off in 6 to 8 hours, leaving no unpleasant results, although there may be some mental confusion in some individuals. In some cases there may be no drowsiness, but, rather, a period of excitement resembling alcoholic intoxication[1]. With the larger toxic doses, and rarely from the smaller doses, there may be a burning sensation in the mouth, throat, and stomach, and nausea and vomiting may be noted as a result of the local irritant action of the drug. As the chief action of chloral hydrate is to depress and eventually paralyze the central nervous system, the patient falls into a deep sleep, from which he cannot be aroused to complete consciousness. The reflexes are lessened or even abolished, the muscles are completely relaxed, the pulse is scarcely perceptible, the blood pressure is lowered, the respiration is irregular and shallow, the face may be pale or flushed, and later cyanotic, the pupils are contracted, often to pinhole size, the extremities are cold, the temperature may fall, convulsions and delirium may occur, and, eventually, fatal asphyxia occurs from paralysis of the respiratory center, or death may result from pulmonary edema. In some non-fatal cases, the coma may last for many hours, even as long as 72 hours[2]. "In some cases, especially in conditions of weakened heart action, as in delirium tremens, the insomnia of continued fevers, etc., death may result very rapidly from failure of the heart[3]; in some cases it occurs even before drowsiness is noticed."

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[1] Fuller, Lancet, 1871, **1**, 403.

[2] See Minot, Boston Med. and Surg. Jour., 1871, **74**, 184; and Benjamin, Charité Ann., 1897, **24**, 249.

[3] See Ingals, Chicago Med. Jour. and Exam., 1877, **34**, 234; and Hunt and Gettler, "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 634.

In the chronic types of poisoning there may be disturbances of digestion, with diarrhea, and loss of weight. The skin, in many cases, may show a scarlatina-like rash. The eyes may show signs of irritation, such as itching, redness, swelling, and excessive excretion. The nervous symptoms include sleeplessness, indefinite pains, general depression, and even melancholia or a condition resembling paretic dementia. Sudden withdrawal of the drug may lead to symptoms resembling delirium tremens; while sudden death is not uncommon among habitues following doses little larger than those to which the subject is accustomed.

Fatal Dose.—As the effects of chloral hydrate vary to some extent with different individuals and even with the same person at different times, it is a difficult matter to state the fatal dose of this drug. Further, the toxic dose of chloral hydrate is, to some extent, dependent upon the age and physical condition of the subject, children apparently bearing its effects relatively better than adults, while elderly individuals, especially if affected with weak hearts, may show marked symptoms from small doses. Thus, 0.194 gram has proven fatal in ten hours to an infant 1 year old, while 2.98 grams has caused the death of a child of 5 years[1]. Death of adults has occurred from doses of 20 grains (1.3 grams)[2], 45 grains (2.9 grams)[3], 60 grains (3.9 grams)[4], and 80 grains (5.2 grams)[5]. On the other hand, recovery has followed the taking of much larger doses. Thus, recovery has taken place from 430 grains (28 grams)[6], from 1 ounce (30 grams)[7], from 1.1 ounces (34.2 grams), and from 3 ounces in 24 hours[8]. Blyth[9] says "It appears tolerably plain that most people would recover, especially with appropriate treatment, from a single dose under 8 grams, but anything above that quantity taken at one time would be very dangerous, and doses of 10 grms. and above, almost always fatal."

Fatal Period.—This is very variable, the average duration of a fatal poisoning running between 8 and 12 hours. Death has been reported in 15 minutes[10], in 20 minutes[11], in 30 minutes[12], while other cases have lingered for 48 hours[13] and even as long as 3 days.[14]

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[1] Cited by Blyth, *Poisons, Their Effects and Detection*, 4th Ed. 1906, p. 165.

[2] See Hart, Med. Rec., 1871–2, **6**, 164; and Ashbaugh, cited by Ingals, Chicago Med. Jour. and Exam., 1877, **34**, 234.

[3] Fordyce, Weekly Med. Rev., 1883, **8**, 94.

[4] Finnell, Med. Rec., 1871–2, **6**, 91; Maschka, Wien. med. Wchnschr., 1871, **21**, 1163.

[5] Ludlow, Med. and Surg. Reporter, 1888, **58**, 596.

[6] Stone, Louisville Med. News, 1883, **15**, 179.

[7] Clapp, Comm. R. I. Med. Soc. 1876, **1**, 83; Hutchinson, Lancet, 1879, **2**, 487; Madigan, Chicago Med. Rev., 1881, **4**, 447; Springthorpe, Austral. Med. Jour., 1887, n. s. **9**, 499.

[8] Cited by Hunt and Gettler, "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 635.

[9] *Loc. cit.* p. 165.

[10] Ingals, Chicago Med. Jour. and Exam., 1877, **34**, 234.

[11] Smith, Boston Med. and Surg. Jour., 1871, **85**, 34.

[12] Hart, Med. Rec., 1871–2, **6**, 164.

[13] Ludlow, Med. and Surg. Reporter, 1888, **58**, 596.

[14] Needham, Jour. Psychol. Med., 1871, **5**, 93.

Treatment.—Chloral hydrate is rapidly absorbed, so that little of the drug will be in the stomach when the patient comes under treatment. The stomach should, however, be washed out with large amounts of warm water, and alkalies may be given in the hope of decomposing any remaining chloral hydrate in the stomach.[1] Strychnine may be given hypodermically, and strong coffee given by mouth or by rectal injection to combat the action of the drug upon the heart, while artificial respiration, with inhalation of pure oxygen, will prove valuable in overcoming the respiratory depression. The body temperature should be maintained by the use of blankets, hot packs, etc.

Postmortem Appearances.—The lesions found at autopsy are not characteristic. The mucous membrane of the mouth, esophagus, and stomach may be reddened and inflamed, while ecchymoses may be found in the stomach. The brain may show hyperemia, while the lungs may be hyperemic or edematous. In chronic cases, there may be fatty degeneration of the heart, liver, and kidney.

Detection.—Chloral hydrate is very prone to decomposition, so that tests for its detection should be made as soon as possible after death, as putrefactive processes have a tendency to decompose it. In the presence of caustic alkali of normal strength the decomposition of chloral hydrate to chloroform and a formate is almost immediate, even in the cold, while N/10 alkali splits it up only slowly in the heat. It follows, therefore, that, even if the tissues are faintly alkaline, chloral hydrate may be recovered in many cases.

The isolation of chloral hydrate from the tissues is accomplished by distillation of the acidified tissues with steam, the process being continued for some time if quantitative results are desired. This distillate will respond to the phenyl-isocyanide, resorcin, naphthol, and pyridine tests as discussed under chloroform on page 711, so that other tests must be employed for differentiation.

1. To a fairly large amount of the distillate add some magnesium oxide and boil the mixture in a flask fitted with a reflux condenser, which process decomposes the chloral hydrate into chloroform, magnesium formate, and water. Heat this mixture on the water-bath to expel the chloroform, make the liquid acid with tartaric acid, and distill off the formic acid. This latter product may be identified either by boiling some of the latter distillate with acidified potassium permanganate solution, when the latter is decolorized; or by heating some of the distillate with a solution of mercuric chloride, when insoluble mercurous chloride is formed.

2. *Phloroglucin Test.*—To 1 cc. of the distillate, add 4 drops of saturated phloroglucin solution and 1 cc. of 20 per cent. sodium carbonate solution, and allow to stand. After about ½ hour a play of colors is noted, lilac to orange, blood-orange, and deep red. If very small quantities of chloral are present, the color change may go only to the orange stage. Chloroform does not give this test, the color developed with chloroform

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[1] See Dougall, Glasgow, Med. Jour., 1895, **43**, 95.

being rather the slight violet of the reagents themselves. Formaldehyde and acetaldehyde give a reddish color, so that these substances should be ruled out by the application of the fuchsin-sulphurous acid test.

3. *Schwarz's Resorcin Test.*—This test, applied as outlined on page 711, gives a reddish color with both chloroform and chloral hydrate, but with chloral hydrate a yellowish-green fluorescence always appears, while with chloroform such a fluorescence practically never occurs, although Schwarz[1] claims that both substances show the greenish fluorescence.

Determination.—An accurately weighed portion of the finely hashed tissue is treated with about ½ its weight of 20 per cent. phosphoric acid solution and distilled with steam for 18 to 20 hours in order to insure the recovery of all the chloral hydrate. If the distillate should be cloudy, it is wise to redistill it to remove possible interfering substances. Render the distillate distinctly alkaline with chlorine-free alcoholic potassium hydroxide solution and heat under a reflux condenser for 5 to 6 hours. Concentrate the liquid on the water-bath, acidify with dilute nitric acid, and precipitate the chlorine with silver nitrate. Filter off the silver chloride and determine its weight in the usual manner. As 3 molecules of silver chloride are equivalent to 1 molecule of chloral hydrate, it follows that 1 mg. of silver chloride represents 0.3845 mg. of chloral hydrate. This method yields accurate results, provided, of course, neither hydrochloric acid nor hydrocyanic acid are present in the distillate.

Detection of Urochloralic Acid.—It is probable that the detection of urochloralic acid in the urine is the most reliable method of deciding as to the presence of a case of chloral hydrate poisoning, especially if the patient does not die.

Evaporate as large a quantity of urine as possible to a syrupy consistency on the water-bath. Strongly acidify with sulphuric acid, and shake out at least three times in a separatory funnel with an alcohol-ether mixture (1:3). Draw off the alcohol-ether layer, and distill off the solvent. Neutralize the residue with potassium hydroxide, and evaporate to dryness. Extract the dry residue with 90 per cent. alcohol, filter, and precipitate the potassium urochloralate with ether. Filter off the precipitate, and wash with ether and alcohol. The precipitate is further boiled with absolute alcohol and filtered hot. Dissolve the potassium salt in a little water, and make the solution just distinctly acid with hydrochloric acid. Shake out this solution with an ether-alcohol mixture (8:1) to remove the alkaline chloride, and draw off the double solvent. Distill off the solvent and treat the residue with moist silver oxide until no more chloride precipitates. Filter off the silver chloride, and remove the excess silver from the filtrate by means of hydrogen sulphide. Filter and carefully evaporate this to a syrup, from which the free urochloralic acid will crystallize out in 18 or more hours in the form of silky, needle-shaped crystals, which melt at 142°C. If these crystals be heated with hydrochloric acid, glycuronic acid and trichlorethyl alcohol are produced. If this mixture be distilled, the glycuronic acid yields furfurol, which appears in the distillate and may be recognized by the formation of an intense red color, if a drop or two of the distillate be brought in contact with a strip of filter paper moistened with a few drops of a solution of aniline acetate.

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[1] Ztschr. f. anal. Chem., 1888, **27**, 668. See Gettler, Proc. Soc. Exp. Biol. and Med., 1919, **16**, 110.

SULPHONMETHANE

Sulphonmethane was introduced by Baumann and Kast in 1888 as a therapeutic agent under the name of sulphonal. Its use as an hypnotic became rather widespread and many medicinal poisonings occurred from overdosage, so that in 1894 Friedländer[1] was able to collect reports of 18 deaths from its use, while in 1900 Taylor and Sailer[2] collated the reports of 34 fatal cases, and Binoth[3] collected 46 cases of sulphonal poisoning in 1903. Since this report, scattered cases have occurred, some of them acute and many of them chronic.[4] Owing to the slight insolubility of sulphonal, absorption is slow and uncertain, so that cumulative effects may follow repeated doses, or long-continued use of relatively small amounts.

Properties.—Sulphonmethane (diethylsulphon-dimethylmethane, sulphonal, $(CH_3)_2C(SO_2C_2H_5)_2$) occurs as colorless, odorless crystals or as a white, odorless powder with practically no taste. One gram of sulphonmethane is soluble in 365 cc. of water, 60 cc. of alcohol, 11 cc. of chloroform, and in 64 cc. of ether at 25°C. It is soluble in 16 cc. of boiling water and in 3 cc. of boiling alcohol. Sulphonmethane melts between 124° and 126°C., and when strongly heated decomposes with the evolution of sulphur dioxide. Its saturated aqueous solution is neutral to litmus paper. It is volatile with steam.

Symptoms.—The general action of sulphonal is much the same as that of paraldehyde or chloral hydrate, but its effects are produced much more slowly and are more uncertain, owing to its slight solubility. It is not uncommon, therefore, to note that the depression and sleepiness are often marked on the day following the administration of the drug. Medicinal doses cause, as a rule, simply a feeling of malaise followed by sleep, which may last for several hours with no further signs. In some individuals, however, there may be nausea and vomiting, headache, dizziness, and muscular weakness resulting in an unsteady gait. With larger doses the symptoms vary with different individuals. There may be marked mental confusion, motor disturbances, even paralysis of the extremities, hyperesthesia, vomiting of bile-containing fluid, abdominal pain, general weakness, stupor, and insensibility. In some cases there may be excitement associated with tonic or clonic convulsions. As the intoxication proceeds, the respiration becomes stertorous and irregular, the pulse very weak, with death from respiratory failure, or, occasionally, from anuria. There may be a slight rise in temperature and various types of skin eruptions may be noted. The urine may contain albumin, bile, red blood cells and casts, while quite commonly, especially in the protracted cases or following frequent use of the drug, the urine may be deep red in color, due to the presence of hematoporphyrin, an iron-free product indicative of the destruction of red blood cells. This pigment is not found in all cases, apparently being more common in cases of anemic women, in whom the symptoms may be very severe.

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[1] Therap. Monatsh., 1894, 8, 231.

[2] Contributions from Pepper Laboratory, 1900, p. 120.

[3] "Ueber Sulfonal und Trionalvergiftung", Dissert., Frieburg, 1903.

[4] See Waldo, Brit. Med. Jour., 1901, 1, 1473; Hind, Lancet, 1904, 1, 219; and Rogers, Jour. Amer. Med. Assoc., 1912, 58, 1510.

In the chronic cases, resulting from long continued use of the drug, headache, vomiting, constipation, hallucinations and other mental disturbances, motor paralysis, and hematoporphyrinuria are prominent symptoms[1], skin eruptions being more common than in the acute form of poisoning.

Fatal Dose.—The fatal dose is variable, depending much on the general condition of the subject. Death has not infrequently followed doses varying from 5 to 30 grams[2], while Gadamer[3] states that it has occurred from 2 doses of 0.9 gram taken within 1½ hours, and Pettit[4] reports a case of death following the intake of 2 doses of 0.97 gram each taken within 1¼ hours. It is not unusual for death to occur following the long continued use of small amounts, such as 0.64 gram daily for several months[5]. On the other hand recovery has followed the taking of such large amounts as 93 and 100 grams[6].

Fatal Period.—Death may occur in a few hours or days[7], or may be delayed for months.

Treatment.—The stomach should be washed out with warm water, and elimination stimulated, both through the kidneys and bowels. Infusions of alkaline saline solutions may prove very valuable. Cardiac stimulants should be used to support the heart, and artificial respiration should be employed when respiratory failure appears imminent.

Postmortem Appearances.—These are not characteristic. There may be some pulmonary congestion, and the kidneys may show evidences of irritation.

Detection.—Sulphonal is decomposed in the body and is excreted largely as ethylsulphonic acid in the urine, although sulphonal itself, occurs in the urine after rather large doses of the drug. The elimination of unchanged sulphonal may continue for several days, the urine, in many cases, being colored dark red from the presence of hematoporphyrin. Sulphonal resists putrefactive processes quite well, so that it may be found in the tissues some time after death. The organs especially suited for its detection are the stomach and bowel, with their contents, the liver, kidney, and brain, while the blood will contain its quota.

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[1] See Bresslauer, Wiener med. Blätter, 1891, p. 3 and 19; de Schweinitz, Therap. Gaz., 1897, **21**, 671.

[2] See Hunt and Gettler, "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 658.

[3] *Lehrbuch der chemischen Toxikologie*, 2te. Aufl., 1924, p. 452.

[4] Medical News, 1889, **55**, 165.

[5] See Pollitz, Wien. klin. Wchnschr., 1898, **2**, 566. See, also, Waldo, Brit. Med. Jour., 1901, **1**, 1473; and Rogers, Jour. Amer. Med. Assoc., 1912, **58**, 1510.

[6] Neisser, Deutsch. med. Wchnschr., 1891, **17**, 702; and Gadamer. *Loc. cit.*

[7] See Knaggs, Brit. Med. Jour., 1890, **2**, 955.

The sulphonal may be isolated from the tissues by the following method. Extract the finely hashed tissues two or three times with alcohol on the water-bath and filter. Distill off the alcohol from the combined filtrates, take up the syrupy residue with boiling water and filter. This aqueous solution is repeatedly shaken out with petroleum ether to remove fats and coloring matter, the purified solution then being shaken out with chloroform, as advocated by Kippenberger, or slightly alkalinized with potassium hydroxide and shaken out with ether, as suggested by Vitali. On evaporation of the solvent the sulphonal will be left as a crystalline residue. If necessary these crystals may be further purified by taking up with hot water or alcohol and allowed to crystallize. With these crystals the following tests may be performed.

1. If a little of the crystalline residue be heated with an equal amount of powdered charcoal in a test tube, the characteristic, unpleasant odor of mercaptan will be noticed, while the vapors will change blue litmus to red from the presence of acetic and formic acids, and the sulphur dioxide also formed will bleach a piece of filter paper moistened with blue starch iodide. Both trional and tetronal give this test, also.

2. If sulphonal be heated with a little powdered iron, the odor of mercaptan develops, and the residue yields hydrogen sulphide on treatment with hydrochloric acid. The same results are given by both trional and tetronal.

3. When the suspected crystals are melted with potassium cyanide, the odor of mercaptan develops and the aqueous solution of the residue yields a red color on the addition of ferric chloride, due to the presence of potassium sulphocyanate. This test must be performed with care, owing to the markedly toxic properties of the potassium cyanide used.

4. If some of the crystalline residue be heated in a test tube with an equal amount of sodium salicylate, an odor of mercaptan develops. If this mixture be treated with a few drops of alcohol and a few drops of concentrated sulphuric acid, allowed to stand for a few minutes, again treated with a few more drops of sulphuric acid and heated, a turbid red solution results, which has the odor of methyl salicylate.

5. As the above tests are not characteristic of sulphonal, being given by both trional and tetronal as well, it is necessary for absolute identification to determine the melting point of the crystalline residue, which must be, of course, pure. The melting point of sulphonal is between 124 and 126°C., that of trional between 74 and 76°C., and that of tetronal between 86 and 89°C.

Estimation.—The extraction of an accurately weighed portion of the finely hashed tissue is made as outlined above, care being taken to insure as complete extraction as possible. The purified residue obtained by either solution in ether or chloroform is dried and weighed.

TRIONAL AND TETRONAL

Trional (diethylsulphon-methylethylmethane, $(CH_3)(C_2H_5)C(SO_2C_2H_5)_2$) is official under the name of *sulphonethylmethanum*, while tetronal (diethylsulphon-diethylmethane, $(C_2H_5)C(SO_2C_2H_5)_2$) is unofficial. Both of these compounds are similar in chemical properties to sulphonal, but are somewhat more readily soluble in water than is the latter compound and both have a bitter taste. Both these hypnotics have caused fatal poisoning[1], but the cases are relatively few.

The symptoms and method of action of these compounds are practically the same as those shown by sulphonal. The methods of isolation and detection have been discussed above.

BARBITURIC ACID DERIVATIVES

The barbituric acid derivatives are probably more widely used at the present time than any of the other sedatives and hypnotics, and find wide application, also, in augmenting the action of such analgesics as aspirin, phenacetine, and pyramidon. They are somewhat more active hypnotics than is chloral hydrate, although their action is somewhat slower in manifesting itself, while this is much more rapid than that of the sulphonal derivatives.

Among the barbituric acid derivatives we find the following: Barbital, soluble barbital, and phenobarbital are official. Sodium phenobarbital, ipral (calcium ethylisopropylbarbiturate), neonal (N-butylethylmalonylurea), and phanodorn (cyclohexenyl ethyl barbituric acid) find inclusion in New and Nonofficial Remedies. Proponal (dipropylbarbituric acid), dial (diallylmalonylurea), allonal (a combination of allylisopropylbarbituric acid and amidopyrine), and amytal (isoamylethylbarbituric acid) are employed less frequently than the other derivatives mentioned.

BARBITAL

Barbital was introduced into medical practice as a hypnotic in 1903 under the name of veronal. It was immediately accepted by the profession, as well as by the laity, and has found wide usage. As was to be expected many cases of untoward effects or actual poisoning arose as a result of overdosage or accident. As early as 1905 Kress[2] reported a number of such cases, and since that time the number of poisonings has

[1] See Young, Univ. Med. Mag., 1896–97, **9**, 715; Church, Amer. Med., 1901, **2**, 729; Hart, Amer. Jour. Med. Sci., 1901, **121**, 435; Laitman, Boston Med. and Surg. Jour., 1924, **191**, 491; Hofmann, *Lehrbuch der gerichtlichen Medizin*, 11te. Aufl., 1927, p. 908.; Krischner, Deutsch. Ztschr. f. d. ges. ger. Med., 1928, **12**, 483.

[2] Ther. Monatsh., 1905, **19**, 467.

rapidly increased, due, possibly, to the fact that veronal can be obtained without a physician's prescription and, also, to the increasing use of hypnotics. In England and Wales, according to Hunt and Gettler[1], it occupied in 1911–13 seventh place in the list of deaths from all poisons. Some of the cases have been of a suicidal nature, Sieveking[2] stating that veronal was taken for this purpose in 45 cases in Hamburg between 1904 and 1913. Many reports of chronic poisoning are finding their way into the literature, owing to the fact that elimination of the drug is slow and cumulative effects are prone to arise.[3]

Properties.—Barbital (diethyl-barbituric acid, diethyl-malonylurea, barbitone, veronal, $CO(HN.CO)_2C(C_2H_5)_2$) occurs as colorless or white crystals, or a white crystalline powder. It is odorless, has a slightly bitter taste, and is stable in the air. Barbital melts between 187° and 190°C. One gram of barbital is soluble in 130 cc. of water, 14 cc. of alcohol, 75 cc. of chloroform, 35 cc. of ether at 25°C., and in 13 cc. of boiling water. It is also soluble in acetone, and in ethyl acetate. A saturated aqueous solution is acid to litmus. It forms salts with alkalies which are soluble in water, the sodium salt being official under the name of *Barbitalum solubile* (barbital sodium, sodium diethylbarbiturate, sodium diethylmalonylurea, barbitone sodium, veronal sodium, medinal). This latter compound is a white, odorless powder with a bitter taste. It is stable in the air and its aqueous solution is alkaline to litmus. One gram of soluble barbital is soluble in 5 cc. of water at 25°C., and in 2.5 cc. of boiling water. Slightly soluble in alcohol and insoluble in ether.

Symptoms.—In the usual therapeutic doses barbital induces sleep with practically no untoward symptoms except in especially susceptible individuals. The symptoms of the toxic action are variable[1], the picture being usually one of depression of the central nervous system, while in other cases there is a mixture of depression and stimulation. In the early stages there may be dizziness, fulness in the head, headache, foul breath, occasionally nausea and vomiting, disturbance of the gait, weakness, mental confusion, disturbance of speech characterized by a slurring, occasionally inarticulate type of expression, and loss of memory. Then follow deep unconsciousness with absence of most of the reflexes, shallow, feeble respiration, often assuming the Cheyne-Stoke type, occasionally stertorous, cyanosis, temperature ordinarily subnormal although it may be somewhat elevated. The pupils are often constricted, while in some cases alternate constriction and dilatation (hippus) may be observed, while transitory paralysis of the external orbital muscles may result in diplopia. The pulse is usually good, full, equal and regular, although in some cases it may be weak and slow. In some cases the coma may be associated with considerable restlessness, exaggerated reflexes, opisthotonos, trismus, and tonic spasms of the neck muscles[2]. Occasionally polyneuritis with patches of dry gangrene of the sole, heel and tips of some of the toes may be observed[3]. The urine may, in some cases, show albumin, blood, or sugar, and, often, hematoporphyrin. Various types of skin eruptions may be observed. The coma may continue for several days, after which the patient may recover, or death may result from respiratory failure, pneumonia, or nephritis.

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[1] "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 660.

[2] Vrtljschr. f. ger. Med., 1918, **56**, 163.

[3] Some of the cases reported during the latter years are the following: Willcox, Lancet, 1913, **2**, 734 and 1178; Alexander, Brit. Med. Jour., 1913, **2**, 20; Garfol, Gazz. d. osped., 1914, **35**, 1960; Lazell, Denver Med. Times, 1914–15, **34**, 261; Husemann, Allg. Ztschr. f. Psychiat., 1915, **72**, 43; Schneider, Ibid., 87; Schubiger, Cor.-Bl. f. Schweiz. Aerzte, 1916, **46**, 1741; Fog, Ugeskr. f. Laeger, 1917, **79**, 370; Oppenheim, Deutsche Ztschr. f. Nervenhkde., 1917, **57**, 1; Gautier, Rev. med. de la Suisse Rom., 1918, **38**, 641; Römer, Deutsche med. Wchnschr., 1919, **45**, 1305; Moszeik, Med. Klin., 1920, **16**, 233; Fleischer, Deutsche med. Wchnschr., 1920, **46**, 630; MacLeod, Med. Rec., 1920, **98**, 985; Taub, Jour. Amer. Med. Assoc., 1920, **74**, 459; Hassin and Wien, Ibid., 1920, **75**, 671; Littell, Ibid., 1921, **77**, 1333; Boenheim, Med. Klin., 1921, **17**, 1263, Hage, Vrtljschr. f. ger. Med., 1921, 3s., **62**, 19 and 223; Vergely, Jour. de med. de Bordeaux, 1921, **92**, 279; Indemans, Nederl. Tijdschr. v. Geneesk., 1922, **1**, 397; Bloch et Deglaude, Paris Méd., 1922, **12**, 276; Bofinger, Deutsche med. Wchnschr., 1922, **48**, 1518; Mantelin, Lyon Méd., 1922, **132**, 295; Cole, Jour. Amer. Med. Assoc., 1923, **80**, 373; Sands, Ibid., 1923, **81**, 1519; Herz, Deutsche med. Wchnschr., 1923, **49**, 416; Brandt, Ibid., 1924, **50**, 1203; Tardieu, Rev. de Méd., 1924, **41**, 393; Ipsen, Wien. med. Wchnschr., 1924, **74**, 2025; Leake and Ware, Jour. Amer. Med. Assoc., 1925, **84**, 434; Rivet, Jany, and Herbain, Bull. Soc. méd. des hôp. de Paris, 1925, **49**, 276; Caussade and Tardieu, Ibid., 295; Scott, Lancet, 1925, **1**, 658; Pucher, Bull. Buffalo Gen. Hosp., 1925, **3**, 70; Lange and Guttmann, Klin. Wchnschr., 1926, **5**, 1655; Stone, Ohio State Med. Jour., 1927, **23**, 132, Paolini, Riforma med., 1928, **44**, 1069; Ruhberg, Minnesota Med., 1929, **12**, 75.

In the *chronic cases*, which result from continued use of small doses over a period of time, the cumulative action of barbital is shown by symptoms which may resemble those of alcoholic intoxication. In such cases the breath is foul and peculiar in odor, nausea is more or less common, there is disturbance of speech characterized by a peculiar slurring or drawling and indistinct enunciation, with frequent omission of letters or syllables. There are mental confusion, loss of memory, hallucination, or even delusions, tremors, ataxic gait, and marked emotional instability[4]. The subject is weak and drowsy and has a tendency to pass into a state of heavy sleep. Skin rashes and trophic disturbances appear much more commonly than in the acute types of poisoning. The wide usage of barbital compounds by the laity for insomnia and nervous disorders has lead to the condition known as barbitalism or veronalism among many of the psychopathically inferior members of society, so that this drug must be accredited with distinct habit-forming properties[5]. Possibly, the solution of the point involved here may be the restriction of the sale of barbital only on physician's prescription.

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[1] See Pollitzer, Jour. Cutan. Dis., 1912, **30**, 185.

[2] See Dargein and Doré, Bull. Soc. méd. des hôp, de Paris, 1927, **43**, 1392.

[3] See Claude, Lamache, and Daussy, L'Encephale, 1927, **22**, 439.

[4] See Sands, Jour. Amer. Med. Assoc., 1923, **81**, 1519; Leake and Ware, Ibid., 1925, **84**, 434.

[5] See Work, Arch. Neurol. and Psychiat., 1928, **19**, 324.

Elimination of barbital is mainly by the kidney, from 50 to 90 per cent. being recovered from the urine, the larger the dose the less the relative percentage excretion, while the remainder is apparently oxidized in the system. The excretion is, however, somewhat slow, occasionally not reaching its maximum until the second day and continuing through the third or fourth day, or even as long as ten days, following the administration of a single dose[1]. It has, moreover, been shown[2] that it is not justifiable to attempt to draw definite conclusions of the intake of barbital from the amount excreted in the urine. The finding of barbital in the urine serves as a practically certain method of differentiating barbital poisoning from such conditions as cerebral hemorrhage, lethargic encephalitis, uremic coma, and alcoholic or other poisoning with which it might be confused.

Fatal Dose.—This depends greatly on the rapidity with which treatment is instituted and upon the state of health of the subject. According to Willcox[3] the smallest dose that has caused death is 0.65 gram (10 grains), the same author citing a case of death from 15 grains. In other cases death has occurred from such doses as 7 grams[4], 8 grams[5] 10 grams[6], and higher dosages. On the other hand, recovery has occurred from doses of 6 grams[7], 8 grams[8], 8.3 grams[9], 9 grams[10], and 21 grams[11]. The average minimum fatal dose, according to Willcox, may be taken as 3.3 grams (50 grains), but this would seem to be somewhat too low, the ordinarily fatal dose running somewhere between 5 and 10 grams, although 1.5 to 3 grams might be fatal to individuals with weak constitutions.

Fatal Period.—Death rarely occurs before 20 hours[12], while it has occurred in 24 hours[13], 36 hours[14], 46 hours[15] 72 hours[16], 79 hours[17], and in

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[1] See Fischer and Hoppe, Münch. med. Wchnschr., 1909, **56**, 1429; Reinert, Arch. exp. Path. und Pharm., 1928, **130**, 49; and Kühn, Deutsche Ztschr. f. d. ges. ger. Med., 1929, **13**, 115.

[2] Reiche, Klin. Wchnschr., 1926, **5**, 2112.

[3] Lancet, 1913, **2**, 734 and 1178. See, also, Cushny, *Pharmacology and Therapeutics*, 9th ed., 1928, p. 252.

[4] MacLeod, Med. Rec., 1920, **98**, 985.

[5] Zörnlaib, Wien. med. Wchnschr., 1906, **56**, 2454.

[6] Weitz, Festschr. d. allg. Krankenh. St. George, Hamburg, 1912; Schröder, Deutsch. Ztschr. f. d. ges. ger. Med., 1929, **13**, 353.

[7] Alexander, Brit. Med. Jour., 1913, **2**, 20.

[8] Hald, Centralbl. f. Nervenhkde. und Psych., 1904, **27**, 369.

[9] Chitty, Lancet, 1913, **1**, 1917: Munroe, Brit. Med. Jour., 1914, **1**, 854.

[10] Hald, *Loc. cit.*

[11] Leake and Ware, Jour. Amer. Med. Assoc., 1925, **84**, 434.

[12] Ehrlich, Münch. med. Wchnschr., 1906, **53**, 559 (2 cases of suicide, one from 11 grams, the other from 15 grams).

[13] Zörnlaib, Wien. med. Wchnschr., 1906, **56**, 2454.

[14] Embden, Münch. med. Wchnschr., 1908, **55**, 1050.

[15] Schneider, Prager med. Wchnschr., 1907, **32**, 17.

[16] Zörnlaib, *Loc. cit.;* Cole, Jour. Amer. Med. Assoc., 1923, **80**, 373.

[17] Germann, Jour. Amer. Med. Assoc., 1906, **46**, 1999.

8 days[1], while recovery has occurred after 6 days of coma. The average period elapsing before death occurs is, probably, about 3 days.

Treatment.—If the drug has been recently taken, the stomach should be thoroughly washed out. Cardiac and vascular stimulants should be pushed. Infusion of normal saline or proctoclysis (Murphy drip) with Fischer's solution should be freely employed. Fluids should be freely given by mouth, if possible, to aid in the excretion through the kidneys. High colonic irrigation may be of value in increasing elimination through the bowels. The urine may need to be drawn by catheterization. Artificial respiration with oxygen inhalations may be called for.

Postmortem Appearances.—The changes found at autopsy are not characteristic. There is general hyperemia of practically all the internal organs, pulmonary edema, cardiac dilatation, usually a bronchopneumonia, and some cerebral edema. The liver may show fatty changes, while the kidneys ordinarily show extensive degeneration of the epithelium of the convoluted tubules, with petechial hemorrhages in the pelves.

Detection.—As stated above, barbital is largely excreted in the urine, so that this fluid offers an excellent opportunity of detecting the existence of a poisoning during life. After death, most of the organs contain their quota of barbital, the kidneys, brain (especially the thalamus and corpus striatum), liver and spleen showing the largest relative amounts in the order named. In a case reported by Pucher[2] the following amounts were isolated: urine, 276 mgs.; kidneys, 47 mgs.; brain, 196 mgs.; liver, 154 mgs.; spleen, 17 mgs.; gall bladder, 5 mgs.

For qualitative purposes veronal may be isolated from the tissues by the following procedures. The finely ground tissue is slightly acidified with dilute hydrochloric or sulphuric acid and extracted with 95 per cent. alcohol in a flask on a steam bath for about an hour. The filtered alcoholic extract is evaporated to a thick syrup, which is taken up with hot water, and filtered. Allow the filtrate to cool and shake this out several times with ether or ethyl acetate. On distilling off the solvent, the barbital will remain behind as a crystalline residue, which may be purified by taking it up with a little hot acidified water, heating to boiling and adding sufficient 5 per cent. potassium permanganate solution to give a slight pink color. Filter and decolorize the filtrate by the addition of a few drops of hydrogen peroxide. Shake out the filtrate with ether or ethyl acetate and distill off the solvent, when the barbital will be quite pure.

If the urine is to be examined, evaporate as large a quantity as can be obtained to a syrupy consistency, and extract this residue thoroughly with acidified alcohol. The further steps are the same as those outlined above. Some workers advise the purification of the ether residue by taking up with hot water and decolorizing with animal charcoal. While this procedure purifies the barbital to a large extent, yet there is considerable loss of material from adsorption, so that this method cannot be used where the quantities are small.

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[1] Schröder, Deutsch. Ztsch. f. d. ges. ger. Med., 1929, **13**, 353.

[2] Bull. Buffalo Gen. Hosp., 1925, **3**, 70. Abs. in Arch. Path. & Lab. Med., 1927, **3**, 893.

With the residue obtained after the final purification the following tests may be performed for identification of barbital.

1. Determine the melting point of the dry crystals. These should melt between 187° and 190°C., but, often, the presence of impurities lowers the melting point quite appreciably.

2. Dissolve some of the crystals in a small amount of warm water and add a few drops of Millon's reagent, or of mercuric nitrate solution, when a gelatinous white precipitate is formed, which is soluble in an excess of the reagent.

3. The crystals of barbital are soluble in solutions of alkali hydroxides, and to a less extent in their carbonates. If such solutions are acidified with hydrochloric or sulphuric acid, barbital is precipitated unchanged.

4. If some of the crystalline residue be boiled with an excess of sodium carbonate solution, the barbital is decomposed with evolution of ammonia.

5. *Van Ittalie and van der Veen's Test.*[1]—Dissolve a little of the suspected residue in water rendered very faintly alkaline with ammonia, and add to this an equal volume of ammoniacal silver nitrate solution[2], when a white precipitate rapidly forms, which redissolves in hot water, and recrystallizes on cooling in definite, colorless, birefringent crystals.

6. *Fabre's Test*[3].—Dissolve some of the suspected residue in a little acetic acid at the temperature of the water-bath. Add an amount of xanthydrol about twice the weight of the barbital, and warm the mixture on the boiling water-bath. Allow to cool, when a crystalline residue slowly forms. At the end of 2 to 3 hours, carefully separate the crystals and wash 3 times with a small amount of boiling 95 per cent. alcohol. Dry the colorless, prismatic crystals and determine the melting point, which should be from 245° to 246°C. The crystals formed by phenobarbital according to this procedure melt at 218° to 219°C., while those derived from diallylmalonylurea melt at 242° to 243°C.

Estimation.—The method outlined above may be used for quantitative determination of the amount of barbital in the tissues or urine. Weighed portions of the finely hashed organ, or a definite volume of urine concentrated to a small volume, are taken and extracted two or three times with boiling acidified alcohol. After filtering the extracts, the combined filtrates are evaporated to a syrup, and this syrup taken up with acidified water and shaken out with petroleum ether to remove fats and other impurities. After separation of the petroleum ether, which is discarded, the aqueous solution is shaken out two or three times with ether, or, as recommended by Van Ittalie and Steenhauer, with ethyl acetate. Withdraw the solvent and evaporate it off on the water-bath. The residue is taken up with about 10 cc. of boiling water and 5 cc. of 5 per cent. sulphuric acid added, and the solution heated to boiling with sufficient 5 per cent. potassium permanganate to give a slight pink color. Filter hot and decolorize the filtrate with a few drops of hydrogen peroxide. Extract this solution again with ether or ethyl acetate, withdraw the solvent, and filter it through a dry filter paper into a weighed beaker. Evaporate the solvent, dry the residue at 95° to 100°C. to constant weight, when the amount of barbital in the quantity of organ extracted is obtained.[1]

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[1] Jour. de Pharm. et de Chim., 1920, **20**, 397.

[2] A 5 per cent. silver nitrate solution to which just sufficient ammonia is added to redissolve the precipitate of silver oxide first formed.

[3] Jour. de Pharm. et de Chim., 1922, **26**, 241. See, also, Lyons and Dox, Jour. Amer. Chem. Soc., 1929, **51**, 288, for a similar test based on the condensation of barbituric acid compounds with p-nitrobenzyl chloride in the presence of sodium carbonate.

PHENOBARBITAL

Phenobarbital (luminal) was introduced in 1913 and has grown in popularity so rapidly, that it is, possibly, the most commonly used sedative and anticonvulsant available. In spite of its wide application in cases of insomnia, general nervous disorders, and in epilepsy, relatively few cases of poisoning have been reported in the literature. Most of the toxic reactions observed have been manifested by the urticarial or measles or scarlatina-like maculopapular erythema, which may follow a single dose or, more usually, repeated doses. In 1928 Menninger[2] summarized reports of 41 cases taken from the literature, which showed toxic reactions characterized by skin eruptions, and added 3 cases of his own. In the case of Hamilton, Geiger, and Roth[3], in addition to the skin eruption the toxic reaction was characterized by severe conjunctivitis. With exception of the case reported by Wright[4], there is only one other fatal case in the literature, that of Hueber[5], but there seems to be some doubt as to this latter case, as death may have been due to the flaring up of an old tuberculous condition.

Properties.—Phenobarbital (Phenylethylmalonylurea, phenylethylbarbituric acid, luminal, $CO(NHCO)_2C(C_2H_5)C_6H_5$) occurs as white, glistening, small crystals, or as a white, crystalline powder, which is odorless and stable in the air. A saturated aqueous solution of phenobarbital is acid to litmus paper. One gram is soluble in about 1000 cc. of water, 8 cc. of alcohol, 40 cc. of chloroform, 13 cc. of ether, and in about 700 cc. of benzene at 25°C. It is soluble in solutions of alkali hydroxides and alkali carbonates, forming, when sodium hydroxide is employed, luminal sodium (phenobarbital sodium, luminal soluble), which finds inclusion in New and Nonofficial Remedies. Phenobarbital melts between 172° and 174°C.

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[1] See Van Ittalie and Steenhauer, Pharm. Weekblad, 1921, **58**, 864 and 1062; and van Rijn, Ibid., 1928, **65**, 1030.

[2] Jour. Amer. Med. Assoc., 1928, **91**, 14. Complete bibliography is given.

[3] Ill. Med. Jour., 1926, **49**, 344.

[4] Arch. Int. Med., 1929, **43**, 85.

[5] Münch. med. Wchnschr., 1919, **66**, 1090. The report of the Chief Medical Examiner of New York for 1926 shows 3 cases of luminal poisoning, but no details are given.

Symptoms.—Phenobarbital is a more active hypnotic and sedative than is barbital. The sleep is deep, and may be preceded by a period of excitement. While toxic symptoms are perhaps less frequent than with barbital itself, yet nausea, vomiting, dizziness, disturbances of speech and vision, unsteadiness, ataxia, diminished reflexes, and, especially, a toxic eruption of the skin, appearing first on the chest and becoming more or less generalized in the form either of an urticarial eruption or of a maculo-papular erythematous morbiliform or scarlatiniform rash[1]. In a case of attempted suicide by the taking of 2.4 grams, deep coma, loss of reflexes, anesthesia, and marked depression of the heart and respiration, with long-continued amaurosis were noted[2]. Death is, probably, due to respiratory paralysis, although there are not sufficient clinical records upon which to base a definite conclusion. Huddleson[3] calls attention to the frequency of subacute and chronic epigastric pains following continued use of phenobarbital.

Fatal Dose and Period.—This can not be stated, as the fatal case of Heuber is questionable, and followed daily doses of 0.5 gram for 30 days, a total of 15 grams, while the other reported fatal case, that of Wright, was caused by an unknown amount.

Treatment.—This is practically the same as that outlined under barbital. For the toxic eruption, prompt removal of the drug, the use of local sedatives and the use of measures to increase general elimination usually prove effective.

Postmortem Appearances.—These are, presumably, much the same as those mentioned under barbital. Necropsy findings have not been reported in man, the fatal case of Wright being worked out from the chemical rather than the pathological standpoint.

Detection.—While the distribution of phenobarbital has not been worked out, it probably follows much the same laws as does barbital, so that the brain, especially the thalamus and corpus striatum[4], would contain the largest amount, with the kidneys, liver and spleen following in the order named. In contradistinction to barbital, phenobarbital does not seem to be excreted in the urine, at least in any such amounts as in cases of barbital poisoning, the percentages found in the urine ranging from 0.18 per cent. to 20 per cent. over a period of days[5], while Wetselaar[6] and Wright[1] report that phenobarbital is not found in the urine in acute poisoning.

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[1] See Farnell, Jour. Amer. Med. Assoc., 1913, **61**, 192; Haug, Münch. med. Wchnschr., 1919, **66**, 1494; Stein, Therap. Halbsmonatschr., 1920, **34**, 387; Jackson, Jour. Amer. Med. Assoc., 1927, **88**, 642; and Menninger, Ibid., 1928, **91**, 14.

[2] Ungár, Wien. klin. Wchnschr., 1914, **27**, 847.

[3] Jour. Amer. Med. Assoc., 1929, **93**, 1637.

[4] See Keeser and Keeser, Arch. f. exp. Path. und Pharm., 1927, **125**, 251.

[5] See Luce and Feigl, Therap. Monatschr., 1918, **32**, 236; Fleury and Guinnebault, C. R. Soc. de biol., 1925, **93**, 1508; Reiche, Klin. Wchnschr., 1926, **5**, 2112; Halberkann and Reiche, Münch. med. Wchnschr., 1927, **74**, 1450; Reinert, Arch. f. exp. Path. und. Pharm., 1928, **130**, 49.

[6] Pharm. Weekblad, 1922, **59**, 521. See, also, Nolte, Pharmaz. Zeitung, 1920, **65**, 320.

In extracting phenobarbital from the tissues, much the same procedure may be used as with barbital. The finely hashed tissues may be extracted for about an hour with hot acidified alcohol, or, as advised by Wright, with plain ether without acidification. The extract is filtered and concentrated to a small volume. If this residue be treated with dilute alkali and shaken out with ether, the sodium salt of phenobarbital, being practically insoluble in ether, will remain in the aqueous layer, while much of the fatty impurity will pass into the ether. Now acidify the aqueous solution with acetic acid and again extract with ether, which will remove the phenobarbital and leave in the aqueous layer the soluble soaps and split products of protein, as shown by Wright[2]. Allow the ether to evaporate spontaneously, when the phenobarbital obtained is, usually, sufficiently pure for the tests. If it is deemed advisable, the above processes may be repeated to insure a practically pure product. In the extraction of phenobarbital from the brain, it is well to evaporate the original ether extract almost to dryness, take up with a very small amount of ether, and pour this ethereal solution into a large volume of alcohol, to remove much of the fats and cephalin. Filter and remove the alcohol by evaporation, take up the residue with acetone, which dissolves the phenobarbital but leaves behind the lecithin. Filter, evaporate off the acetone, and take up the residue in ether. Filter if necessary to obtain a clear solution, and allow the ether to evaporate, when the phenobarbital will be obtained quite pure.

If the above processes be conducted upon a weighed portion of the tissues, and the processes are carefully carried out, the final ether extract may be filtered into a weighed beaker, and the quantity of phenobarbital in the tissue taken determined by weight of the dry residue. With the crystalline residue obtained in the above process, the following identification tests may be made.

1. Determine the melting point, which should be, if the residue be pure, between 172° and 174°C., but, as usually obtained, this will be found to be about 170°C. Mixing the residue with an equal amount of known phenobarbital and determining the melting point of the mixture, will add confirmatory evidence as to the identity of the residue, providing the melting point is not appreciably depressed.

2. *Ranwez's Test*[3].—To a small amount of the suspected residue add about 5 times the amount of potassium nitrate and about 2 cc. of concentrated sulphuric acid and boil for 10 minutes. Pour the yellow solution into 10 cc. of cold water, when a heavy crystalline precipitate appears. On now adding a large excess of ammonia to this mixture, the precipitate

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[1] Arch. Int. Med., 1929, **43,** 85.

[2] Arch. Int. Med., 1929, **43,** 85.

[3] Jour. pharm. Belg., 1924, **6,** 410.

dissolves and an intense yellow solution results. This test is, according to Ranwez, given only by malonylurea derivatives containing the aromatic ring.

3. *Ekkert's Test.*—To a small amount of the suspected residue, add about 1 cc. of formaldehyde and 4 cc. of concentrated sulphuric acid, and place the mixture on the water-bath. In a short time the mixture acquires a brilliant rose-red color, then a wine-red color, if phenobarbital is present. With barbital and proponal only a yellowish color develops[1].

HYDROCYANIC ACID

Hydrocyanic acid and its alkali salts, sodium and potassium cyanides, are used quite extensively in the arts, in electro-metallurgical processes, in metallurgy, in photography, and, also, to a very limited extent in medical practice. Free hydrocyanic acid, liberated by the action of strong acids upon the alkali cyanides, has found somewhat wide application as a disinfecting and parasiticidal agent, and has been frequently employed in fumigating apartments, ships, etc.[2] It is found in such industrial gases as illuminating gas and blast furnace gas, and is formed in the distillation of coal-tar and in the fumes from burning celluloid[3]. It appears to exist preformed in the juice of the cassave (*Manihot utilissima*) and in all parts of the Javanese tree, *Pangium edule.* In the form of certain glucosides this acid occurs in a large number of plants, in over 180 species it is said[4], and in certain liquors derived from them, as, for instance, maraschino, and cherry, apricot, plum, and other brandies. As amygdaloside (amygdalin) it is found in the bark, leaves, flowers, and fruit of cherry laurel, and in plants of the genera *Prunus*, *Cerasus*, *Sorbus*, *and Spiroea*[5], and in the seeds of cherry, plum, peach, apricot, apple, and pear. According to Lange[6] the amounts of amygdaloside in these common seeds are as follows: peach, 2 to 3 per cent. (0.11 to 0.16 per cent. HCN); plum and apricot, 1 per cent. (0.05 per cent. HCN); apple, 0.6 per cent. (0.03 per cent. HCN), and cherry, 0.8 per cent. (0.04 per cent. HCN). Amygdaloside is present, also, in bitter almonds to the extent of about 3 per cent. (0.16 per cent. HCN), and in the official Oil of Bitter Almonds (*Oleum Amygdalae Amarae*), the Pharmacopoeia directing that there shall be not less than 85 per cent. of benzaldehyde and not less than 2 per cent. and not more than 4 per cent. of hydrocyanic acid in this preparation, although the amount found in many crude preparations varies widely from this figure[1]. Amygdaloside is by itself usually harmless, but it is readily hydrolyzed by the ferment emulsin, which ordinarily accompanies it in nature, as well as by other ferments, probably even by the intestinal ferments[2], into hydrocyanic acid, benzaldehyde, and glucose, according to the equation

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[1] Pharm. Zentralhalle, 1926, **67**, 481.

[2] See Hamilton, *Industrial Poisons in the United States*, 1925, p. 344.

[3] See Kockel, Vrtljschr. f. ger. Med., 1903, **26**, 1.

[4] See Kobert, *Lehrbuch der Intoxikationen*, 2te. Aufl., 1906, **2**, 836; Dunstan, Henry and Auld, Proc. Roy. Soc., London, 1907, **79, B**, 315; Armstrong, Ibid., 360; and Compton, Chem. News, 1912, **106**, 163.

[5] See Witthaus, *Tocicology*, 1911, p. 792.

[6] Arch. Kais. Ges. Amt., 1907, **25**, 478.

$$C_{20}H_{27}NO_{11} + 2H_2O = 2C_6H_{12}O_6 + C_6H_5CHO + HCN.$$

Other cyanophoric glucosides are known, which have in certain instances resulted in death, especially to animals which have eaten plants containing them. Thus, phaseolunatoside, derived from *Phaseolus lunatus* (commonly known as Rangoon, Burma, Indian, Java, Moon, etc. beans) has proven fatal in cases reported from Germany and Porto Rico, owing to the liberation of hydrocyanic acid in the intestinal tract after eating the beans. These beans contain from 8 to 56 mg. HCN per 100 grams of bean, although there appears to be a somewhat wide variation in the figures reported by various investigators[3]. Beans containing any appreciable amount of HCN are not allowed to be imported into the United States[4]. Among other cyanogenous glucosides we find lotusoside in *Lotus arabicus*, dhurroside, in *Sorghum vulgare* (millet), linamaroside from the seeds of flax (*Linum usitatissimum*), sambunigroside, from elder (*Sambucus nigra*) gynocardoside, from *Gynocardia odorata*, and vicianoside, from various species of vetch[5]. Besides this occurrence of these cyanogenous glucosides in plants, we find that certain myriapods contain hydrocyanic acid as secretory products of certain glands.

It has been shown by Aders-Plimmer[6] that HCN is formed by oxidation of protein *in vitro*, so that it is quite probable that such formation may occur normally in the body, the amounts, however, being small and not leading to poisoning owing to the rapid detoxication of the HCN by combination with sulphur, liberated at the same time from the decomposing protein, to form the thiocyanate, which is excreted in the saliva and the urine. Sensi and Revello[7] have shown that hydrocyanic acid is formed in the body during putrefaction, while Patty[8] has demonstrated its formation by the action of *Bacillus pyocyanus* on protein.

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[1] The Pharmacopoeia states that "this oil is intended for medicinal use and neither it nor its solution should be used or sold for flavoring foods," owing to the fact that the crude oil of bitter almonds was widely used as a flavoring agent and had lead to poisoning. At present the "synthetic oil of bitter almonds," which is benzaldehyde with no hydrocyanic acid, has taken its place. This latter compound must not be confused with the "artificial or false oil of bitter almonds," which is nitrobenzene and is distinctly poisonous.

[2] See Gerard, C. R. Soc. de Biol., 1896, 2 s., **2**, 44.

[3] See Lührig, Chem. Ztg., 1920, **44**, 166 and 262; Wirthle and Rheinberger, Ztschr. f. Unters. d. Nahrungs -und Genussmittel, 1920, **39**, 346; Sudendorf and Gahrtz, Ibid., 350; Gabel and Küger Münch. med. Wchnschr., 1920, **67**, 214; Grimme, Pharm. Zentralh., 1920, **61**, 159; Grumme, Fortschr. d. Med., 1920, **37**, 124.

[4] U. S. Dept. of Agr., Bur. of Chem. Serv. and Reg. Ann., 1917, No. 20.

[5] See Kobert, *Lehrbuch der Intoxikationen*, 2te. Aufl. ,1906, **2**, 839; and Witthaus, *Toxicology*, 1911, p. 793.

[6] Jour. Physiol. 1904, **31**, 65.

[7] Ann. chim. applicata, 1926, **16**, 268. Abstract in Chem. Abs., 1926, **20**, 3469.

[8] Jour. Inf. Dis., 1921, **29**, 73.

Owing to the varied uses of hydrocyanic acid and the cyanides, these agents are readily accessible to the public and have been employed as poisons in many cases all over the world. Indeed, as stated by Hunt and Gettler[1], "in the statistics of some European countries they occupy the third or fourth place in the order of frequency with which death is caused by poisons." In 426 cases reported in England for 10 years ending in 1892, 344 cases were suicidal, 38 were accidental, 14 were homicidal, and 30 were of unknown classification. In the ten years ending in 1903, there were in England and Wales 536 recorded cases of poisoning with hydrocyanic acid or cyanides, of which 481 were suicidal, 54 accidental, and 1 homicidal; while for the years 1912 to 1913 there were 166 cases, of which 153 were suicidal and 13 accidental. In 1876–78 there were in Berlin 40 cases of cyanic poisoning out of a total of 432 poisonings from various sources, while in 1903 there were 38 such cases reported in the German statistics. In our own country, we find there were 135 cases reported in the registration area in1909, 120 of which were suicidal and 15 accidental. Of 30 fatal cases occurring in St. Louis from 1910 to 1914, 28 were suicidal and 2 accidental. In New York City in 1925 there were 18 suicidal and 4 accidental cases, while in 1926 there were 14 suicidal and 1 accidental poisonings from cyanides. In the collation of 492 cases by Witthaus[2] in 1911, there were reported in the literature 295 suicidal, 123 accidental, 36 homicidal, 10 homicidal and suicidal (simultaneously), and 28 undetermined cases. Of these 194 were by hydrocyanic acid, 154 by potassium cyanide, 65 by oil of bitter almonds, 9 by eating bitter almonds, 10 by cherry-laurel water, 38 from unusual sources, such as almond cake, prussian blue, potassium ferrocyanide followed by an acid, almond flavor, gilding solution, sherry brandy, fruit seeds, etc., and 22 of unknown origin. Larsen[3] reports the death of a girl of 16 from swallowing some "Cinderella Silver Slipper Cream" and points out the danger of using such preparations for cleaning purposes. Hydrocyanic acid itself seems to be used for suicidal purposes, especially by physicians, chemists, and pharmacists, while the cyanides are employed by photographers, electroplaters, and the general public.

The use of hydrocyanic acid as an insecticide has lead to a number of deaths in various parts of the world, although such methods have been employed in the United States since 1886. Many of these cases do not find their way into the records, so that it is not possible to give any statistics on the subject. The records of the Public Health Service cover the cases occurring in the fumigation of vessels under supervision of that service. These records show, according to Hamilton[4], that there were 3 deaths in 1916, then none till 1920, and between June, 1920, and

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[1] "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 674.

[2] *Toxicology*, 1911, p. 797.

[3] Hospitalstid., 1928, **71**, 1104.

[4] *Industrial Poisons in the United States*, 1925, p. 346.

July, 1923, there were 18. In Cleveland 4 deaths were reported from such a source, while in Chicago 6 deaths have followed improper fumigation with HCN[1]. In the Krupp works in Essen 10 men died from the fumes of HCN, with which the living rooms of the men were being fumigated[2].

As previously mentioned hydrocyanic acid is formed by burning celluloid. It is stated by Kockel[3] that 8 deaths occurred from this source in Leipzig in 1900. It is possible that some of the effects in the recent disaster in Cleveland, in which many persons lost their lives from the fumes of burning *x*-ray films, may have been due to hydrocyanic acid, but it is more probable that most of the cases, at least, died from the effects of nitric fumes.

Most of the cases of hydrocyanic acid poisoning have occurred from the ingestion of the acid itself, or from the alkali cyanides and the preparations containing amygdaloside. A few cases, however, have been reported from the actual inhalation of the fumes of the gas, especially those arising from the use of the gas as an insecticide or vermicide. In the cases arising from the intake of mercuric cyanide, the action of both the mercury and cyanogen ions is noted, so that the case may assume the characteristics of one or the other of these poisonous substances in any particular instance. Thus, in the famous Molineux[4] case, the symptoms were largely those of mercuric poisoning, while another case occurring about the same time in New York City[5] showed the rapid effects of cyanide poisoning. While the double cyanides, potassium ferrocyanide, Prussian blue, Turnbull's blue, etc., are ordinarily non-toxic, yet, when taken in conjunction with acids, these compounds exert the usual fatal effects of hydrocyanic acid. "Cyanic acid, the cyanates, and the sulphocyanates are nearly harmless. Cyanogen, cyanogen iodide, cyanogen chloride, and nitroprussiate of soda are not very poisonous."[6]

Properties.—Hydrocyanic acid (Prussic acid, formonitrile, hydrogen cyanide, HCN) is a colorless, transparent liquid of a peculiar, penetrating, quite characteristic odor resembling that of peach kernels. It has a specific gravity at 18°C. of 0.697, boils at 26.5°C., and solidifies at -15°C. It volatilizes very rapidly, and is quite unstable, becoming more or less rapidly decomposed by exposure to light to ammonium formate. The *Acidum hydrocyanicum dilutum* (formerly official) is a 2 per cent. aqueous solution of the acid, but rarely held its strength owing to decomposition. At present the only official preparations containing HCN are the *Oleum amygdalae amarae* (oil of bitter almond), which should contain not less than 2 and not more than 4 per cent. hydrocyanic acid, and the preparations of *Prunus virginiana* (wild black cherry bark).

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[1] See McNally, Medical Jour. and Rec., 1924, **119**, 143.

[2] Führer, Deutsch. med. Wchnschr., 1919, **45**, 847. See, also, Koelsch. Zentralbl. f. Gewerbehyg., 1920, **8**, 93 and 101.

[3] Vrtljschr. f. ger. Med., 1903, **26**, 1.

[4] 168 N. Y., 264.

[5] See Witthaus, *Toxicoloby*, 1911, p. 743.

[6] Hunt and Gettler, "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology*, 1923, **2**, 685.

Potassium cyanide (KCN) is a white, deliquescent salt, odorless when perfectly dry, but having the odor of HCN when moist. It is readily soluble in water, the solution having an alkaline reaction. The salt usually contains more or less potassium carbonate, arising from the absorption of carbon dioxide of the air. Potassium cyanide is readily decomposed by acids, even by carbon dioxide, with elimination of HCN.

Sodium Cyanide (NaCN) occurs in the form of white, opaque, amorphous fragments, or as a white granular powder, which is non-deliquescent. It is readily soluble in water with alkaline reaction. During the war this salt largely replaced potassium cyanide, as the potassium was especially required for purposes of warfare. The toxic effects of these alkali cyanides are the same as those of the equivalent amount of HCN which they contain.

Symptoms.—Hydrocyanic acid acts as a poison upon almost all forms of living matter. It is, in fact, a true protoplasmic poison. Its action is due, as was shown by Geppert[1], to its influence in retarding oxidative processes. As a consequence of this action the tissues are no longer capable of absorbing oxygen,[2] while the blood in the higher animals retains its oxygen, so that both the arterial and venous blood are bright red in color. The symptoms of poisoning are, therefore, in reality, those of an internal asphyxiation of the tissues in the presence of an excess of oxygen. The central nervous system is first stimulated and then paralyzed. The stage of stimulation is, usually, very short, and is associated with excitement and convulsions, the latter resembling those produced by stimulation of the hind-brain, while the subsequent paralysis appears to include all parts of the central nervous system. The respiration is rendered quicker and deeper in the beginning, but later becomes irregular, weak, and finally ceases. The circulation is primarily stimulated, the action on the inhibitory center slowing the pulse, while the increased activity of the vasoconstrictor center causes a primary rise in blood pressure. Soon, however, the depression of the vasomotor center lowers the blood pressure, and the heart itself shows the toxic effects, the pulse becoming weak and irregular.

The action of hydrocyanic acid upon the blood is due to the fact that the peroxidase present in the blood is rendered inert, so that no effervescence occurs when hydrogen peroxide is added to blood containing hydrocyanic acid, and the hemoglobin is changed into methemoglobin. It is probable that during life no direct combination of hydrocyanic acid with hemoglobin occurs, the bright red color of the venous blood being due to the fact that the oxyhemoglobin is not reduced.

Hydrocyanic acid is readily absorbed from all mucous membranes and, also, from external surfaces, so that poisoning may occur from inhalation, from absorption from the rectum, vagina, stomach, and other mucous surfaces, as well as from application to the intact skin. A part of the poison taken into the system is excreted unchanged through the lungs, while some of it is rapidly converted into sulphocyanides and excreted, as such, in the urine. A further possibility of detoxication of hydrocyanic acid is the combination with the aldehyde group of the sugar of the blood and tissues. It is possible, also, that HCN may be oxidized or hydrolyzed by ferments and converted into ammonium formate.

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[1] Ztschr. f. klin. Med., 1888, **15**, 208 and 307.

[2] See Dixon and Elliott, Biochem. Jour., 1929, **23**, 812.

"The symptoms of hydrocyanic acid poisoning vary according to the size of the dose and the purity of the preparation taken, and also with the condition of the stomach, whether empty or containing food". When large quantities, either of the acid itself or of the salts, are taken the symptoms begin almost at once, rarely being delayed for more than a few minutes. In some cases the patient may utter a shrill cry, but this is by no means universal, and then fall down insensible. Convulsions are common, but after large doses death may be so rapid that these do not appear. The respiration is at first rapid and convulsive, but soon becomes slow and gasping. The pulse is at first rapid, but soon becomes weak and imperceptible.

With smaller, but fatal, doses, the course is slightly prolonged. The patient notices the hot, acrid, bitter taste of the poison, and complains of a feeling of constriction in the throat. The further symptoms may follow rapidly, although in many cases the subject may be capable of performing slight voluntary acts[1]. The convulsive stage now follows. "The feeling of constriction in the throat is followed by salivation, nausea, and, occasionally, though rarely, by vomiting; these are followed by anxiety, confusion, vertigo, and headache. There are unsteadiness of the gait and a feeling of stiffness of the lower jaw. There are palpitation of the heart and a feeling of constriction in the chest, and the respiration becomes first rapid, then slow and irregular. The inspirations are very short, the expirations greatly prolonged. The patient becomes unconscious, falls suddenly to the ground in convulsions not unlike those of epilepsy. The skin is covered with a cold sweat; the pupils are dilated and insensible to light; the eyes are glassy, staring, and very prominent, as in other cases of asphyxia. The mouth is covered with foam, which is sometimes blood-stained; the breath smells strongly of hydrocyanic acid. The pulse is at first rapid, but so weak that it can scarcely be felt. The convulsions may be general and lead to opisthotonos, or they may be confined to certain groups of muscles; thus there is often trismus. The hands are usually clenched. Involuntary evacuations of the feces and urine, also of the semen, may occur."[2] This convulsive stage is followed by the paralytic or asphyctic stage. The patient remains comatose; the skin becomes cyanotic; the temperature falls; the heart is weak and irregular, and the blood pressure falls; while the respiration shows marked effects, due to the paralysis of the medullary center, the respiration ceasing for long periods, followed by a short, gasping inspiration and, later, by a prolonged expiration, which is succeeded by slow and shallow breathing and final cessation. Death usually follows when the respiration becomes greatly depressed, but, in some cases, recovery follows improvement in the respiratory symptoms, this recovery being usually rapid, but, occasionally, symptoms of weakness and drowsiness may continue for a few days.

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[1] See Hickman, Lancet, 1866, **1**, 310.

[2] See Hunt and Gettler, "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 677.

In cases of poisoning with potassium or sodium cyanide, there may be local symptoms of marked gastric irritation, as a result of the corrosive and irritating action of the alkaline carbonates, which these salts may contain. Recovery is, as a rule, slower with these salts than with the acid itself, and vomiting commonly occurs early following intake of the alkaline cyanides, while after ingestion of the acid vomiting is somewhat rare, except in the stage of recovery. It is to be said that the action of the cyanides is the same as that of an equivalent amount of hydrocyanic acid. The same may be said with reference to other hydrocyanic acid-containing compounds, such as the oil of bitter almond.

Chronic Poisoning.—As Hamilton[1] remarks, "Chronic cyanide poisoning from HCN and its compounds is certainly rare and there are even skeptics who refuse to believe that any indubitable cases have ever occurred." Practically all cases of so-called chronic cyanide poisoning have resulted from inhalation of the gas, whether of the pure gas itself or from that generated by the action of acids upon the alkali cyanides. If the inhalation of large quantities has occurred, the case is one of acute poisoning, the symptoms being rapidly developed and almost immediate unconsciousness following. The chronic type of poisoning occurs among gilders, photographers, silver polishers and cleaners, and other industries employing hydrocyanic acid or its salts, although such workers as Fühner[2] and Koelsch[3] have not found such cases among operatives. The symptoms which have been noted are oppression of the chest, throat irritation, headache, vertigo, paleness of the face, loss of appetite, nausea and vomiting, weakness, offensive breath, and dyspnea. In some cases it has been characterized by severe gastro-intestinal disturbance, vomiting, abdominal cramps, obstinate constipation, and by general functional disturbance of the nervous system.[4] In one case, that of an Italian silver polisher, the illness came on suddenly with symptoms of meningitis lasting 4 or 5 days, and then passed leaving a loss of power in the legs and arms, but with no sensory symptoms, this loss of power lasting for 6 months and then slowly improving.[1] In a case of poisoning in which death resulted in 2 weeks following a massive dose of potassium cyanide, Ernst[2] raised the question as to whether this may not be a case of chronic poisoning, but it is highly probable, as Raestrup[3] states, that this is really an acute case with delayed death.

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[1] *Industrial Poisons in the United States*, 1925, p. 348.

[2] Deutsch. med. Wchnschr., 1919, **45**, 847.

[3] Zentralbl. f. Gewerbehyg., 1920, **8**, 93 and 101.

[4] See Martin, Friedreich's Bl. f. ger. Med., 1888, **39**, 3; Merzbach, Hyg. Rundschau, 1899, **9**, 45; Nalan, Jour. Amer. Med. Assoc., 1908, **50**, 365; and Reed, Jour. Ind. Hyg., 1920, **2**, 140.

Fatal Dose.—It is probable that the amount of hydrocyanic acid, which may be inhaled in the air without causing death, is greater than is often stated. Of course, in considering this question, the time of exposure must be a factor as well as the concentration of the gas. Thus, Starkenstein,[4] basing his statements upon the early work of Lehmann, Hess and of Zangger, asserts that 0.2 to 0.3 mg. of HCN per liter of air is immediately fatal; 0.12 to 0.13 mg. per liter may prove fatal if breathed for ½ to 1 hour. "In experiments with rats made by the United States Public Health Service 1.0 part per 1000 killed in 10 minutes, 0.5 part failed to kill in that time, and 0.1 seemed to be safe for rats. Men at rest stood 0.25 part per 1000 for two minutes, and 0.375 for a minute and a half without dizziness. Even 0.5 was endured for one minute without injury."[5] Longer exposure to these concentrations would, unquestionably, lead to severe and fatal results.

It is probable that the average lethal dose of hydrocyanic acid taken by mouth is about 60 cg. (1 grain), which corresponds to about 3 cc. of the 2 per cent. solution of hydrocyanic acid, 0.154 gram (2.4 grains) of potassium cyanide, to about 50 bitter almonds, and to 1.5 to 3 cc. of the oil of bitter almonds. The smallest dose of hydrocyanic acid known to have caused death is 1.87 cc. of the 2 per cent. solution,[6] while recovery has followed the ingestion of 15 cc. of this 2 per cent. solution.[7] Potassium cyanide has caused death in doses of 0.13 gram (2 grains)[8], while doses as large as 3.25 grams (50 grains)[9] have been recovered from. Owing to the variation in the amount of hydrocyanic acid in the older preparations of the oil of bitter almond, it is difficult to state just how much of this acid was contained in the fatal doses reported. Taylor[10] records a case of a woman who died in ½ hour from 17 drops of the oil, while doses as large as 22.5 cc. (6 drams) have been recovered from[11].

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[1] Collins and Martland, Jour. Nerv. and Ment. Dis., 1908, **35**, 417. See, also, Rosenbloom, Jour. Lab. and Clin. Med., 1923, **8**, 258.

[2] Deutsch. med. Wchnschr., 1928, **54**, 1373.

[3] Ibid., 2179.

[4] "Blausäure und die Zyanide" in *Toxikologie* by Starkenstein, Rost and Pohl, 1929, p. 243.

[5] Hamilton, *Industrial Poisons in the United States*, 1925, p. 346.

[6] Garstang, Lancet, 1888, **2**, 15.

[7] Kolipinski, Maryland Med. Jour., 1898, **40**, 24.

[8] Bennett, Med. Rec., 1894, **45**, 742.

[9] Gillebrand, Lancet, 1876, **2**, 223.

[10] *On Poisons*, 3rd Amer. Ed., 1875, p. 587.

[11] Allen, Int. Med. Mag., 1893, **2**, 126.

Fatal Period.—The action of hydrocyanic acid is very rapid. In many cases, especially those following ingestion of large doses, the interval between the taking of the poison and unconsciousness is a matter of seconds, rather than of minutes. This rapidity of action does not preclude, however, the possibility that a person receiving a fatal dose of hydrocyanic acid or its salts may perform some conscious act. Thus, in a case reported by Howard[1], the victim was able to scrawl 8 words in an attempt to make a will, and, further, walked from the back room of his grocery store to tell a customer to call later. The average duration following large doses is, probably, from 2 to 10 minutes, while with smaller doses life may be prolonged for ½ hour. As a rule recovery follows if the patient lives an hour, although there are reports of cases in which death did not occur for 1 hour and twenty minutes,[2] and even as long as 3½ hours after taking the fatal dose[3]. Death may occur from the alkali cyanides, or the oil of bitter almonds, as rapidly as from hydrocyanic acid itself, but cases are reported in which death has been delayed as long as 24 hours[4], and, in one case, 12 days after onset of symptoms.[5]

Treatment.—In the rapid cases following intake of large amounts of the free acid or, oftentimes, of the salts, little is to be expected from any line of treatment; indeed, the physician usually does not arrive till death has occurred. If the patient is still alive, the stomach should be immediately washed out, using water containing 0.3 per cent. potassium permanganate, hydrogen peroxide, a mixture of ferrous sulphate and ferric chloride, or, as advocated by Martin and O'Brien,[6] a mixture of ferrous sulphate and magnesium oxide. It is probable that the washing out of the cyanide remaining in the stomach is the valuable part of this procedure, as the conversion of the cyanide into the oxamide or ferrocyanide is, probably, too slow to be of much value. If bitter almonds or seeds containing amygdaloside have been taken, it is wise to attempt to empty the stomach by ordinary emetics in order to remove the large particles which would clog the stomach tube, Lang[7] has advocated the hypodermic or intravenous injection of sodium thiosulphate in the hope that the harmless sulphocyanide might be formed, but the results have been unsatisfactory in most cases. The intravenous injection of glucose[8] may prove of value by combining with the cyanide and removing some

[1] Boston Med. and Surg. Jour., 1927, **196,** 58. See Hickman, Lancet 1866, **1,** 310.

[2] Garstang, Lancet, 1888, **2,** 15.

[3] Brit. Med. Jour., 1883, **1,** 131.

[4] See Edelmann, Deutsch. Ztschr. f. Nervenhkde., 1921, **72,** 259.

[5] Ernst, Deutsch. Med. Wchnschr., 1928, **54,** 1373.

[6] Proc. Soc. Chem. Ind., Victoria, 1901, **1,** 119.

[7] Arch. f. exp. Path. u. Pharm., 1895, **36,** 75. See, also, Hunt, Arch. int. Pharmacod, et de Ther., 1904, **12,** 447; Flury and Heubner, Biochem. Ztschr., 1919, **95,** 249; and Caldas. Bull. assoc. Brazil Pharm., 1927, **8,** 25 (abstract in Chem. Abs., 1928, **22,** 2987); Feyerabend, Klin. Wchnschr., 1928, 7, 1351.

[8] See Violle, Bull. acad. med., 1926, **95,** 664.

of it from the field of action, Forst[1] having shown that glucose alone or glucose plus insulin will protect an experimental animal against 4 times the fatal dose of hydrocyanic acid. Forst, in his investigations, showed that sodium thiosulphate was not especially effective, but that the subcutaneous injection of colloidal sulphur in sodium bicarbonate solution was fairly active. He found that, although it was not always possible to ward off death, the intravenous injection of doses of 6 to 20 cc. of dioxyacetone into an animal protected it against 9 times the fatal dose, while a combination of the dioxyacetone with 3 to 6 cc. of colloidal sulphur effected a complete cure, even when 10 times the fatal dose was administered. This line of treatment should, therefore, offer great possibilities.

Hot and cold douches may be used to stimulate the respiration, while, in the very severe cases, artificial respiration may be employed. Symptoms of collapse should be treated by hypodermics of ether, or strychnine, and other stimulants. In some cases withdrawal of blood from the veins may be practiced, replacing the blood with twice its amount of physiological saline.

Postmortem Appearances.—The autopsy findings following poisoning with hydrocyanic acid itself and with the alkali cyanides are somewhat different. With the former the findings may be almost negative with the exception of the characteristic odor of the acid, which is noted on opening the body, and is especially evident in the stomach, serous cavities, and the brain, Thomas[2] calling attention to its concentration in the lateral ventricles. This odor is, in some cases, sufficiently marked to cause severe irritation of the throat of the pathologist and may, rarely, lead to poisoning[3]. In other cases it is very slight, and may even be absent if putrefaction has proceeded very far. While a somewhat similar odor is noticed in cases of nitrobenzene poisoning, the odor of the benzene compound persists for some time after exposure of the organism while that of hydrocyanic acid is rapidly dissipated. Rigor mortis usually sets in relatively early and may persist for days. The blood is usually fluid and dark in color, especially when death has resulted from asphyxia after some minutes, although, in some cases, it may be partially coagulated, especially in the chambers of the heart, and may be bright red in color. The body may have a natural color, and the livores, especially where death is rapid, may be bright-red in color, instead of the usual gray-violet or violet color of these "death spots"[4]. Thomas[5] calls attention to the pink color of the intestines and gastric mucosa, and the bright pink staining of the intima of the aorta, together with a uniform blue-green color of the liver, and a green color of the gray matter of the brain. Hemorrhages may be noted on the pleurae and pericardium, while the meninges and brain are hyperemic. Bein[1] reports the case of a man showing acute yellow atrophy of the liver following inhalation of hydrocyanic acid.

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[1] Arch. f. exp. Path. u. Pharm., 1928, **128**, 1.

[2] Lancet, 1923, **1**, 1219.

[3] See Mittenzweig, Ztschr. f. Med.- Beamte, 1888, (1), 101.

[4] See Richter, Vrtljschr. f. ger. Med., 1901, **22**, 264; and Laves, Deutsch. Ztschr. f. d. ges. ger. Med., 1929, **13**, 261.

[5] *Loc. cit.*

In cases of poisoning with the alkali cyanides, the above findings will prevail, and, in addition, more or less characteristic appearances are noted in the stomach and intestines. In those cases in which these changes are especially marked, the gastric mucous membrane throughout the stomach, and especially in the fundus and on the tops of the rugae, appears blood-red in color and swollen, even at times appearing almost transparent. The color of the gastric mucous membrane is not everywhere of the same shade, varying between red and red-brown to black-brown.[2] The irritative and even corroding effect observed in the stomach is due to the action of the potassium or sodium carbonate contained in the alkali cyanide, while the coloration noticed is possibly due to the combination of the hydrocyanic acid with the blood pigment, which has been altered by the alkali carbonates. The first of these effects, the hyperemia and corrosion, is, probably, the principal one taking place during life, while the swelling and discoloration is a post-mortem change. It is to be said that these changes occur only when there is sufficient alkali in the ingested cyanide to render the gastric contents alkaline, so that, if the cyanide is administered in acid wines or in lemonade, nothing more than slight swelling and redness may be noted, or even nothing abnormal may be found in the stomach. These same changes may be observed in the duodenum, in the throat and esophagus. About the mouth and in the larynx and trachea may be found a frothy mucus in cases of poisoning with either the free acid or the alkali salts, while the skin about the mouth may show streaks of corrosion where the salts are used.

Detection.—As Hunt and Gettler[3] remark, "There have been undoubted cases of poisoning with hydrocyanic acid where competent chemists were unable to detect the substance a few hours after its use." It is true, however, that the length of time in which hydrocyanic acid may be detected in the organs depends largely upon the extent of putrefaction and the amount of poison taken. While hydrocyanic acid is quite unstable and is soon dissipated when the organs are exposed to the air[4], yet if the organs remain in the body and putrefactive processes are present some of the hydrocyanic acid may remain for varying periods.

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[1] Zentralbl. f. inn. Med., 1924, **45**, 970.

[2] See Hofmann-Haberda, *Lehrbuch der gerichtlichen Medizin*, 11te. Aufl., 1927, p. 893.

[3] "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines, and Webster, 1923, **2**, 685.

[4] Lewis (Jour. South African Assoc. Anal. Chem., 1921, **4**, 19, abstract in Chem. Abs., 1921, **15**, 3431) shows that the loss of HCN is very rapid in unpreserved viscera, all possibly being lost in less than 2 days, yet when the viscera are preserved in alcohol, a slow progressive loss takes place but over half the original quantity of HCN remains at the end of 30 days.

Thus, Autenrieth[1] obtained weighable quantities of HCN from the liver, spleen, kidneys, and heart of a 5 year old child exhumed after being buried for 45 days; and in experiments made with parts of organs and blood to which bitter almond water or potassium cyanide has been added, the same author showed that more than 40 per cent. of the HCN originally added could be obtained even after 60 days, although the mixtures were in a high state of putrefaction. Zillner[2] was able to find hydrocyanic acid in the body of a suicide found 4 months after death. Cram[3] found that not until 76 days had elapsed since death did the stomach contents of a fatal case of potassium cyanide poisoning fail to show a trace of the poison, although the viscera of this same case failed to give a trace of hydrocyanic acid a "short time" after death. In the case reported by Jollyman[4] hydrocyanic acid could be detected in the stomach contents 6 months after death from potassium cyanide poisoning. Struve[5] was able to detect HCN in a mixture of potassium cyanide and meat, which had been kept in a closed vessel for 547 days (18 months).

While hydrocyanic acid may, in some cases, not be detected in the organs sent for analysis, owing (1) to the combination of a portion of the HCN with the aldehyde group of the carbohydrates[6], (2) to the transformation of a portion of it into the sulphocyanate[7], (3) to the possible conversion of a further portion into ammonium formate, and (4) to the actual dissipation of the volatile acid from the tissues, there is still another possibility that must be considered. If the body has been embalmed with formalin prior to the removal of the tissues, or if, as often happens, the tissues are sent to the analyst in formalin, the hydrocyanic acid possibly present in the tissues forms a condensation product with the formaldehyde, the nitrile of hydroxyacetic acid (glycollic acid) being formed. Whether or not hydrocyanic acid may be detectable under these conditions, will depend entirely on the amount of formaldehyde added to the tissues. In ordinary embalming there is, usually, sufficient formaldehyde used to combine with much more hydrocyanic acid than is ordinarily present in cases of poisoning, so that it is possible that the presence of HCN in the embalmed tissues will escape detection. Autenrieth[8] states that "a test for hydrocyanic acid was obtained where liver, containing 0.2 gram of potassium cyanide, was preserved in 1 per cent formalin solution, because the quantity of formalin was not sufficient to combine chemically with the entire quantity of potassium cyanide present." In a recent case examined by the writer, in which the deceased had taken for suicidal purposes a strongly ammoniacal solution of KCN, even though the body had been embalmed before the removal of the organs for examination, appreciable amounts of hydrocyanic acid were obtained from the stomach, kidneys, liver, and spleen which were submitted for analysis. The explanation of this is, probably, that the ammonia combined with the formaldehyde forming methenamine and the hydrocyanic acid partly escaped condensation to the nitrile. Although the chances of detecting hydrocyanic acid are much reduced, and may be rendered impossible, by embalming, yet careful examination should be made in all cases as some evidence of the presence of this acid may be obtained, and special attention should be given the history of the case (if such can be obtained) and the autopsy findings[1].

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[1] Ber. der Deutsch. Pharm. Ges., 1910, **20**, 432.

[2] Vrtljschr. f. ger. Med., 1881, **35**, 193.

[3] Jour. Amer. Chem. Soc., 1914, **36**, 606.

[4] Chemiker-Zeitung, 1905, **29**, 350.

[5] Ztschr. f. anal. Chem., 1873, **12**, 14.

[6] See Kohn-Abrest and Lupu, C. R. Acad. des Sci., 1928, **187**, 362.

[7] See Kohn-Abrest, Ann. méd.-légale et de criminol. police sci., 1929, **9**, 132.

[8] *Detection of Poisons*, 6th Amer. Ed., translated by Warren, 1928, p. 104.

For a chemical examination for hydrocyanic acid and the cyanides, the gastric and intestinal contents are of special importance, while the liver, brain, kidneys and heart all yield their quota of the poison, although, in some cases, none may be found in the brain, heart, or spleen[2]. While the blood usually shows the presence of the cyanide in cases of poisoning, the urine may prove negative, Kobert[3] stating that only once has he found unequivocal evidence of the presence of HCN in human urine.

Preliminary Test.—This test, known as Schönbein's test, is of special value, inasmuch as a negative outcome of the test practically excludes the possibility of the presence of hydrocyanic acid, while a positive result indicates that cyanides may be present. Place a portion of the suspected material in a flask, and acidify with tartaric acid. Close the flask with a tightly fitting cork whose lower surface is provided with a slit into which is inserted a strip of filter paper which has been wet in turn with a 10 per cent. alcoholic solution of guaiac and a 0.1 per cent. aqueous copper sulphate solution and allowed to dry. Now warm the contents of the flask on the water-bath, when a blue or blue-green color of the filter paper will indicate the possible presence of hydrocyanic acid or cyanides. This test is very sensitive, so that a negative result practically rules out of consideration either hydrocyanic acid or the soluble cyanides, while a positive outcome simply indicates that the cyanides may be present, as ammonia, volatile ammonium compounds, hydrochloric acid, nitric acid, chlorine, bromine, hydrogen dioxide, ozone, etc. may, also, cause the treated paper to turn blue. The Schönbein test depends upon the fact that ozone is liberated by the action of hydrocyanic acid upon copper sulphate, and this oxidizing agent promptly oxidizes the guaiac resin, according to the following equation:

$$12HCN + 9CuSO_4 + 3H_2O = 3Cu(CN)_2 + 3Cu_2(CN)_2 + 9H_2SO_4 + O_3.$$

Instead of using paper moistened with guaiac solution, one may employ a solution of benzidin.

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[1] In this connection see Howard, Boston Med. and Surg. Jour., 1924, **190**, 975.

[2] See Stoermer, Deutsch. Ztschr. f. d. ges. ger. Med., 1928, **12**, 251.

[3] *Lehrbuch der Intoxikationen*, 2te. Aufl., 1906, p. 850.

It is possible, in some cases, that the hydrocyanic acid indicated by the Schönbein test may have been derived from the decomposition of the complex cyanides, such as potassium ferrocyanide and ferricyanide, and less likely that it may have come from the splitting up of potassium sulphocyanate. It is wise, and probably necessary, therefore, to determine whether or not these substances are present in the suspected material, before proceeding with the isolation of the hydrocyanic acid. If a portion of the suspected tissue be warmed with water and filtered, the extract will contain the above-mentioned cyanic compounds, if they be present. Acidify the filtrate with hydrochloric acid and divide this acidified extract into 3 parts. To one part add a few drops of a solution of ferric chloride, when a blue color and precipitate of Prussian blue will indicate the presence of a ferrocyanide, while a red color will show the presence of a sulphocyanate. To a second portion of this acidified filtrate add some sodium acetate solution and a few drops of copper sulphate solution, when a red color and precipitate of copper ferrocyanide will confirm the presence of a ferrocyanide. To the third portion of the acidified filtrate add a few drops of ferrous sulphate solution, when a blue color and precipitate of Turnbull's blue will show the presence of a ferricyanide.

Another condition, that must be taken into consideration before one is in a position to start on the isolation of hydrocyanic acid from the tissues, is the possible presence of mercuric cyanide, as the cause of the poisoning in question. Although practically all the cases of poisoning with mercuric cyanide show the symptoms of mercury poisoning, rather than those of cyanide action, yet, occasionally, cases of the latter type do occur. When mercuric cyanide solutions are distilled or heated with tartaric acid, no hydrocyanic acid is evolved unless the amount of the cyanide be large. If, however, a few cc. of freshly prepared hydrogen sulphide water be added and distillation continued, the distillate will contain HCN. It is necessary, therefore, to make a test for mercury (Reinsch test), in order to determine what procedure to follow in isolating the hydrocyanic acid from the tissues.

Having determined by the Schönbein test that hydrocyanic acid is present in the tissues, the method of procedure will depend upon (1) the absence of complex cyanides, (2) the presence of these complex cyanides, and (3) the presence of mercury in the tissues.

Isolation of HCN in Absence of Mercury and Complex Cyanides.—The suspected material is finely hashed, is mixed with water, and is strongly acidified with tartaric acid. This mixture is now submitted to slow distillation over a warm water-bath for 5 or 6 hours, a gentle current of air being passed through the material to facilitate the removal of the HCN. The receiver for the distillate should contain some 5 per cent. potassium hydroxide solution to absorb the volatile gas, and the outlet tube of the condenser should dip under this solution. Instead of using this slow method, one may employ that of distillation with steam, continuing the distillation until about 1 cc. of distillate is collected for each gram of original material used. Care should be taken that the condenser and receiving flask are well cooled, in order to prevent the escape of the volatile acid, as serious results might ensue to the worker from inhaling the gas. The distillate will contain, of course, the HCN in the form of KCN in solution in the excess of potassium hydroxide. Roe[1] advises the aspiration of air through the vessel containing the acidified cyanide solution, the air then being drawn through a solution containing 5 per cent. KOH. He employs about 3 liters of air per minute and continues the aeration for 2 hours.

Isolation of HCN in the Presence of Complex Cyanides.—In the presence of ferrocyanide or ferricyanide of potassium, thoroughly mix the hashed tissue with a sufficient quantity of sodium bicarbonate solution to insure a distinct alkalinity, as advocated by Autenrieth[2], and submit the mixture to slow distillation at a temperature not in excess of 60°C. The fluid in the receiving flask should be a 10 per cent. solution of silver nitrate acidified with nitric acid, instead of the 5 per cent. KOH solution used in the previous method, as HCN may be lost from the distillate when the alkali solution becomes saturated with carbon dioxide. The HCN is precipitated as silver cyanide. Under the conditions of this test potassium cyanide is decomposed by the evolved carbon dioxide, but the compound cyanides do not yield a trace of HCN. This method gives the HCN arising from both the free HCN and the alkali cyanides, while the former procedure yields HCN from the complex cyanides as well. If there is reason to suspect that the complex cyanides are concerned in the poisoning, both the above methods should be employed, and the quantitative difference between the yields of HCN in the two instances will represent the HCN derived from the complex cyanides.

Isolation of HCN from Mercuric Cyanide.—In case the Schönbein test has not shown positive results, and there is reason to believe that the poisoning may be due to mercuric cyanide, the procedure is as follows: Add to the hashed tissue some water and acidify with tartaric acid. To this acidified mixture add hydrogen sulphide water until the mixture smells strong of the gas. Under these conditions the mercuric cyanide is decomposed and the HCN liberated. Distill the mixture, either by the slow process or with steam, as previously discussed, passing the distillate first through a small wash-bottle containing a hydrochloric acid solution of bismuth trichloride to remove the H_2S, and then into either potassium hydroxide solution or a solution of silver nitrate as may be preferred. Roe[3] advises the addition to the hashed tissues of solid sodium chloride followed by tartaric acid solution and then by a solution of stannous chloride to reduce the mercury cyanide to mercurous chloride and metallic mercury. The HCN is then isolated by aeration into 5 per cent. sodium hydroxide solution.

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[1] Jour. Amer. Chem. Soc., 1923, **45**, 1878.

[2] Arch. der Pharm., 1893, **231**, 99.

[3] Jour. Amer. Chem. Soc., 1923, **45**, 1878.

With the distillates obtained by these different procedures, one may perform the following tests for identification of the hydrocyanic acid. If the distillate was received in potassium hydroxide solution, it may be necessary in some tests to neutralize it, while, if the distillate was passed into silver nitrate solution, the precipitated silver cyanide is filtered off, washed with water, suspended in water, and decomposed with hydrochloric acid. Filter off the silver chloride and neutralize the filtrate with potassium hydroxide.

Prussian Blue Test.—A few cc. of the suspected distillate, which may be alkaline or neutral according to circumstances, are treated with 1 or 2 drops of a freshly prepared aqueous ferrous sulphate solution and 1 drop of ferric chloride solution. Unless the original distillate was alkaline, add to this mixture a drop or two of potassium hydroxide solution and warm gently. Now add to this warm mixture sufficient hydrochloric acid to acidify it, when a precipitate of Prussian blue will appear, if the amount of hydrocyanic acid is fairly large. If the quantity be small, the mixture will be blue, blue-green, or green-blue. This test is said to show hydrocyanic acid in a dilution of 1:50,000[1]. According to Vorlander[2] the concentration of hydrochloric acid must be kept down to approximately 0.5 normal, as too much HCl retards the formation of Prussian blue.

Sulphocyanate Test.—A little of the distillate is made alkaline if necessary and a small amount of yellow ammonium sulphide solution is added. Evaporate the mixture to dryness in a porcelain dish on the water-bath, and dissolve the residue in a small amount of very dilute hydrochloric acid. Warm this solution and filter to remove sulphur, repeating the process until a clear filtrate is obtained. Now add to the clear filtrate a few drops of dilute ferric chloride solution, when a deep red color, due to the formation of ferric sulphocyanate, will appear if the distillate originally contained hydrocyanic acid in fairly large amounts, while the coloration will be fainter, but still reddish, in the presence of small amounts. This red color differs from that produced in the presence of meconic acid in that the addition of mercuric chloride solution discharges it, while that due to meconic acid is unaffected. This test was originated by Liebig[3] and is extremely delicate, indicating hydrocyanic acid when present to the extent of 1:4,000,000[4]. Occasionally it happens that this test yields a positive result when other tests for hydrocyanic acid fail, due, probably, to the presence of sulphocyanate originally in the distillate rather than to the conversion of hydrocyanic acid into sulphocyanate during the test. To decide this point the

[1] Link and Möckel, Ztschr. f. anal. Chem., 1878, **17**, 455.

[2] Ber. d. d. chem. Ges., 1913, **46**, 181.

[3] Liebig's Annalen der Chemie, 1847, **61**, 126.

[4] Link and Möckel, Ztschr. f. anal. Chem., 1878, **17**, 455.

distillate should be tested by the addition of dilute hydrochloric acid and ferric chloride without the addition of ammonium sulphide[1].

Nitroprusside Test.—Add to a small amount of the distillate a few drops of potassium nitrite solution, then 2 to 4 drops of ferric chloride solution, and sufficient dilute sulphuric acid to give the mixture a bright yellow color. Heat the mixture to boiling, allow to cool, add sufficient ammonia to precipitate the excess of iron, and filter. On adding to the filtrate a few drops of very dilute ammonium sulphide solution, a violet color will appear, which gradually passes through blue to green and then yellow. This test is due to the formation of potassium nitroprusside, and was originated by Vortman[2], who claims its limit of delicacy to be 1:312,000.

Silver Nitrate Test.—On acidifying the distillate with nitric acid and adding silver nitrate solution a white, curdy, anhydrous precipitate of silver cyanide forms, which is readily soluble in ammonia, sodium thiosulphate, and solution of potassium cyanide. This precipitate may be distinguished from one of silver chloride, with which it might be confused, by the test of Blyth.[3] Filter off the precipitate and thoroughly wash it with alcohol followed by ether. Place the perfectly dry precipitate in a closed or sealed tube, containing a few crystals of iodine. Heat gently, when cyanogen iodide is sublimed in the form of beautiful pale-red needles which condense on the cold part of the tube. These crystals may be dissolved in a dilute solution of potassium hydroxide and the Prussian Blue test performed.

There are many other tests described for the identification of hydrocyanic acid, but none of them are as characteristic as those given above, so that we refer to other works for such methods.

Estimation.—Weigh out a definite portion of the hashed tissue, place in a distilling flask, acidify with tartaric acid and distill as previously described. In the receiving flask place 20 cc. of strong silver nitrate solution acidified with nitric acid. Continue the distillation until no turbidity is produced when the distillate strikes the receiving solution. Collect the precipitate of silver cyanide upon a weighed filter, wash with water until the filtrate comes through free from silver, dry at 100°C., and weigh. The difference in weight between the filter and the filter plus precipitate represents the amount of silver cyanide in the quantity of tissue originally used. Multiply this value by 0.2018 to obtain the equivalent in terms of hydrocyanic acid, or by 0.496 to obtain the amount of potassium cyanide.

In certain cases it is advisable to determine whether the cyanide was in the form of the potassium or sodium salt, as this point may be raised during the investigation. The best method of deciding this point, in the absence of the actual material known or supposed to have been taken, is to ash the organs or the gastric contents and determine the basic constituents according to the known methods of quantitative analysis. A distinct increase in either the sodium or potassium of the tissue points to the probability of the intake of the corresponding cyanide. With this factor, one may calculate the combination of either the potassium or sodium cyanide that may have been found in the tissues.

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[1] See Struve, Ibid., 1873, **12**, 14.

[2] Monatsch. f. Chem., 1886, **7**, 416.

[3] *Poisons: Their Effects and Detection*, 4th ed., 1906, p. 216.

CYCLIC COMPOUNDS

This group comprises a large number of important compounds, many of them being derivatives of the benzene nucleus, while others show a higher or lower number of carbon atoms in the ring. We shall attempt to discuss these compounds in order of their chemical composition rather than under pharmocological groups.

Benzene

The hydrocarbons of the benzene series are ordinarily derived from the dry distillation of coal, and are by-products of the industries such as those of coaking coal and the production of illuminating gas. These hydrocarbons, together with large numbers of complex chemical bodies, are found in the crude coal tars, the different constituents distilling off at variable temperatures. In the usual process of distillation, the "light oils" distill over at temperatures up to 170°C. and consist largely of benzene and its homologues, toluene and xylene mixed with pyridine and thiophene; the fraction distilling between 170° and 230°C. is known as "middle oil" and consists of naphthalene and phenol; the "heavy oil" distills between 230° and 270°C. and is composed of phenol, cresol, anthracene, etc. (the mixture being known as creosote); while the fraction coming over above 270°C. is known as "anthracene oil" or "green oil," and is made up of anthracene, phenanthrene, solid hydrocarbons, etc. These different fractions contain some of the elements belonging to both the higher and lower fractions, so that it is a matter of difficulty to purify the compounds by fractionation.

Benzene (benzol, C_6H_6) is, when pure, a colorless, transparent liquid which has a pleasant, non-irritating odor. It boils at 79.6°C., has a specific gravity of 0.878 at 20°C., and is very inflammable.[1] Its vapors are about three times heavier than air. Besides this pure benzene, there are several commercial grades: (1) the so-called commercially pure benzene, which contains a low percentage of such associated products as toluene, the three isomeric xylenes, the isomeric tri-methyl benzenes (mesitylene, pseudo-cumol, hemimellithol), and other higher homologues, together with thiophene, carbon disulphide, etc.; (2) the 90 per cent. benzene, so called because 90 per cent. distills over at a temperature below 100°C., which contains a larger percentage of impurities; and (3) the 50 per cent. benzene, which contains 50 per cent. of constituents distilling below 100°C. and about 90 per cent. distilling below 120°C. Toluene (methyl benzol) boils at 110.5°C. and has a specific gravity of 0.866, while ortho-xylene boils at 144°C. and has a specific gravity of 0.879, meta-xylene boils at 139°C. and has a specific gravity of 0.865, and para-xylene boils at 137.7°C. and has a specific gravity of 0.861.

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[1] See International Critical Tables.

Benzene has found wide use in the industries, so that it is not strange to find that cases of poisoning have arisen in those exposed to inhalation of its vapors. Hamilton[1] says, "At present, benzene is used in every branch of rubber manufacture, not of course in all departments of every rubber works, but in some department in practically every individual plant. It is a much better solvent for gums, resins, and fats than is any petroleum derivative and it dries faster than high-test gasoline. It is used for cement in shoe factories and in millinery manufacture, in the making of fabrikoid, artificial leather, and linoleum, in coating leather for upholstery and for automobile tops, and as a constituent of shellacs, varnishes, golding and bronzing fluids, varnish and paint removers, and quick-drying paints for interior work. Enormous quantities of benzene rubber mixture are used in the making of so-called sanitary food cans. In the manufacture of pharmaceutical supplies, benzene is used to crystallize out coal-tar drugs. It is the starting point of many important intermediates in dye manufacture, such as aniline, and is also the starting point of synthetic carbolic acid and of the important explosive, picric acid. Copper and zinc are cleaned with benzene in preparation for glavano-plating, and the photoengravers use it to dissolve rubber films. It is also used in the manufacture of kodak and moving picture films." Besides the above uses, benzene has been somewhat extensively used for automobiles.

Poisoning from benzene may arise from its oral ingestion or, more frequently, from its inhalation in the various industrial lines above mentioned, and in chemical laboratories which are called upon to use benzene for various tests. It has been employed for purposes of suicide, and has resulted in quite a number of accidental deaths, but, so far as we can find record, it has never been used for homicidal purposes. There has been some controversy as to the relative toxicity of pure benzene, crude benzene, and such homologues as toluene and xylene. It is believed that pure benzene is more toxic than the crude product, and that benzene possesses greater toxicity than its homologues, although there are some who hold that crude benzene is the more toxic.[2] Owing to the supposed greater toxicity of benzene it has been urged that the homologues be substituted in the industrial processes in order to lessen the hazard, especially from the chronic types of poisoning.[1] McCord[2] believes that there is need of further work with reference to the toxicity of benzene, stating in this connection that, "Up to the present time I have not found any published reports on the action of extraordinarily pure benzene . . . In citing the constant impurities of industrial benzenes, there is no intent to deny or question the actuality of benzene toxicity. It is, however, proper to suggest the likelihood of participation in benzene toxicity of unknown or little known factors, such as impurities, nonsusceptibility and exquisite susceptibility of exposed workmen, and enhancement of benzene toxic properties in certain industries."

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[1] *Industrial Poisons in the United States,* New York, 1925, p. 454.

[2] In this connection see Lewin, Münch. med. Wchnschr., 1900, **48,** 2377; Chassevent and Garnier, Arch. internat. de pharmacol., 1905, **14,** 93; Rambousek, Concordia, 1910, **17,** 448; Hektoen, Jour. Infect. Dis., 1916, **19,** 69 and 737; Harrington, Boston Med. and Surg. Jour., 1917, **177,** 203; Schwenke, Jour. Gasbel, 1920, **63,** 142; Pugliese, Chem. Abs., 1923, **17,** 516; Batchelor, Amer. Jour. Hyg., 1927, **7,** 276.

The cases of acute poisoning are, as might be expected, largely of an accidental nature, arising from exposure to the vapors of benzene under such conditions as distilling benzene without having the condenser sufficiently cooled, spilling large amounts of benzene, cleaning benzene stills, tanks, etc., while many cases have occurred among those attempting to rescue others overcome by the fumes. It is of great importance to remember that even the most thorough cleaning and steaming of the benzene tanks may not be sufficient to remove all the toxic benzene, as many fatal poisonings attest. From the study of many of these cases, it would appear that susceptibility plays a marked rôle in these acute poisonings, as it is not always the one exposed the longest to the fumes that dies. A further point is, of course, the concentration of the fumes in the air to which the person is exposed, while it is of interest to note that exertion seems to increase the severity of the poisoning, as there are quite a few cases in which the one going to the rescue of a stricken fellow workman dies, while the original victim survives.

Symptoms of Acute Poisoning.—Benzene has found some use as a therapeutic agent in the treatment of leukemia, as it has a marked effect in lowering the number of leucocytes in the blood, but it must be stated that it is a difficult matter to control this action, so that, oftentimes, toxic effects arise. When benzene is taken orally in toxic amounts, there is a burning sensation in the mouth and stomach, dizziness, flushing of the face followed by pallor, cyanosis of the extremities, restlessness, dilated pupils, fever, muscular tremors, convulsions, and delirium, which may be followed by narcosis. In other cases, narcosis comes on almost at once, the patient passes into coma, and dies from respiratory failure.

When the vapors of benzene are inhaled in high concentration, the symptoms may come on very rapidly and death follow in a very few minutes,[3] while in other cases the victim may live for some hours, showing the symptoms mentioned above as associated with oral ingestion of the poison.

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[1] See Hamilton, Jour. Amer. Med. Assoc., 1922, **78**, 627; Duvoir, Bull. de la Soc. Méd. des Hôp. de Paris, 1922, **46**, 1541; "Final Report of the Benzol Committee," National Safety Council, May 1925; Winslow, Jour. Ind. Hyg., 1927, **9**, 61; Hamilton, Ibid., 1928, **10**, 227.

[2] Jour. Amer. Med. Assoc., 1929, **93**, 280.

[3] See Sury-Bienz, Vrtljschr. f. gerichtl. Med., 1888, **49**, 138; Beinhauer, Münch. med. Wchnschr., 1896, **43**, 915; Lewin, Ibid., 1907, **54**, 2377; Rambousek, Concordia, 1910, **17**, 448 (cited by Hamilton).

Chronic Poisoning.—While acute benzene poisoning occurs quite frequently in isolated cases, the chronic type of poisoning is more often observed by both the physician and toxicologist and affects many individuals simultaneously in the same plant. These cases follow the continued exposure to fumes of benzene, the time necessary for development of symptoms depending upon the concentration of the fumes and partly upon the susceptibility of the individuals exposed. Some cases show marked symptoms after an exposure of a week or two, while others require some months of exposure to the same concentration. Many of these cases result fatally, Pohl[1] stating that 2 out of 3 such cases terminate in death. Women seem to be somewhat more susceptible to the action of benzene than do men. The difference in susceptibility is shown by the two following reports. Starr[2] described a series of poisonings in which 22 of 27 women, employed in spreading a rubber cement on cloth and pasting it on buckram hat crowns, were affected. The solvent of this cement consisted of about 70 per cent. carbon tetrachloride, 30 per cent. benzene, with traces of carbon disulphide, the cement being kept on the work tables in open tin cups into which the girls dipped their brushes. McCord[3] mentions a group of 40 japanners, who daily spent from 6 to 8 hours coating full sized cowhides with enamels containing up to 60 per cent. benzene, and never less than 25 per cent. This work was done in a room without artificial ventilation and without acceptable natural ventilation. Further, the coated cow hides are dried in the same workroom, and tubs of the benzene-containing enamel and coatings stand open in the immediate vicinity, this situation continuing for a period of more than 10 years. Up to the time of writing his report, McCord was not able to find a record of a single case of benzene poisoning, with the exception of benzene dermatitis, in this plant.

The symptoms of this type of benzene poisoning differ somewhat from those of the acute form, the special activity of the benzene upon the blood and blood-forming organs being prominent points in the symptomatology. The patients may complain of occasional burning in the throat and sometimes in the eyes, headache, dizziness, excitement followed by drowsiness, purpuric spots on the skin, in some cases a dermatitis, and, later, profuse hemorrhages from the gums, nose, stomach, and uterus, and, also, into the skin. There is a progressive anemia, the red cells sinking in some cases to lower than one million per cmm., the cells showing anisocytosis, poikilocytosis, and achromia, but no nucleated red cells being found. There is a coincident lowering of the hemoglobin values. Especially characteristic is the lowering of the number of the leucocytes, the polymorphonuclear neutrophiles being markedly concerned in this leucopenia. The white cells may be diminished to less than 1000 per cmm., and the neutrophiles may be reduced to almost the vanishing point, giving rise to a relative leucopenia with a relative lymphocytosis. There is, at the same time, a diminution of the number of platelets[1]. Along with these findings, there may be observed general weakness, nausea and vomiting, burning in the epigastrium, fever (although this is rarely high), increasing cachexia, and death. Although the hemorrhages and the purpuric spots on the skin are practically constant findings in this type of benzene poisoning, it is probable that the most characteristic feature is the profound leucopenia with a relative lymphocytosis, the lesions being essentially those of aplastic anemia with destruction of the hemoplastic tissue. The coagulation time and the bleeding time of the blood are increased in benzene poisoning, points of importance in differential diagnosis from Schultz's agranulocytic angina, with which it might be confused if the blood findings are made the criterion. In the diagnosis of benzene poisoning a history of sufficient exposure to benzene must obtain, and the symptom complex must be more or less definite. "Persons working with benzene in quantities far below the likely threshold of danger may present to their examining physicians a clinical picture almost exactly like that caused by benzene, without that chemical having contributed in any degree to the causation of the disease."[2]

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[1] "Benzol" in *Toxikologie* by Starkenstein, Rost and Pohl, Berlin, 1929, p. 321.

[2] Jour. Indust. Hyg., 1922, **4**, 203.

[3] Jour. Amer. Med. Assoc., 1929, **93**, 280.

Fatal Dose and Period.—It is difficult to give any exact figures as to the fatal dose of benzene, as the literature is meager on this point. It has been stated[3] that 9 to 12 grams have caused serious collapse, when taken by mouth, while 1 ounce of "nearly pure benzene" has proven fatal in 12 hours[4]. When inhaled death may result rapidly, Beisele[5] reporting a case of death after 4 minutes' exposure from dipping benzene from a bowl, while the cases of Sury-Bienz[1] and of Beinhauer[2] died in "a few minutes" According to the Bureau of Mines[3], 1570 to 3130 parts of benzene per million of air produce only slight symptoms after several hours of exposure; 3130 to 4700 parts per million is the maximum concentration which may be inhaled for 1 hour without serious disturbance; while 19,000 parts per million prove rapidly fatal for even short exposure. These figures are those which produce acute effects, the chronic effects being noted after continued exposure to much lower concentrations. Henderson and Haggard[4] state that no definite figures have been established for the concentrations causing chronic poisonings. "Analyses of the air in factories where poisoning has occurred give values ranging from 5000 down to 200 parts of benzene per million of air." It is probable that especially susceptible individuals would show effects from the lower concentration.

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[1] It should be mentioned that a single blood count should not be relied upon to determine whether or not there is a reduction in the number of either red or white cells, as many workers have shown that there is a normal fluctuation in the number of these cells. As McCord remarks, "The practice of eliminating (temporarily or permanently) all benzene workers on detecting by a single white cell count such numbers as 4,400, 4,800, and 5,000 probably works unjust hardships on worker and employer alike." The same may be said of single red counts.

[2] For reports of some of these cases see Santesson, Arch. f. Hyg., 1897, **31**, 336; Selling, Johns Hopk. Hosp. Bull., 1910, **221**, 33; Beitr. z. path. Anat. u. z. allg. Path., 1911, **51**, 576; Johns Hopk. Hosp. Rep., 1916, **17**, 183; Harrington, Boston Med. & Surg. Jour., 1917, **177**, 203; Legge, Jour. Ind. Hyg., 1919, **1**, 539; Starr, Ibid., 1922, **5**, 203; Faure-Beaulieu and Levy-Bruhl, Bull. et mém. Soc. méd. des Hôp. de Paris, 1922, **46**, 1543; Hogan and Shrader, Amer. Jour. Pub. Health, 1923, **13**, 279; Teleky and Weiner, Klin. Wchnschr., 1924, **3**, 226; Heim, Agasse-Lafont, and Feil, Presse méd., 1924, **32**, 497; Rohner, Baldridge and Hausmann, Arch. Path. and Lab. Med., 1926, **1**, 221; Hunter and Hauflig, Boston Med. & Surg. Jour., 1927, **197**, 292; Smith, Jour. Ind. Hyg., 1928, **10**, 73; Orzechowski, Virchow's Arch; 1929, **271**, 191.

[3] See Hunt and Gettler, "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 691.

[4] Kelynack, Gaz. méd. de Paris, 1893, p. 541.

[5] Münch. med. Wchnschr., 1912, **59**, 2286.

Treatment.—The victim should be removed as rapidly as possible from the exposure, and artificial respiration carried out for some time. In the acute cases, the recovery is usually complete and fairly prompt, if recovery occurs at all, but most of the cases die from respiratory failure. In the chronic cases, blood transfusion seems to be the best treatment, but many patients do not respond even to this. Smith[5] reports some improvement following ingestion of whole liver.

Postmortem Appearances.—In the acute form of benzene poisoning, the body may show many bright red, cadaveric spots, the blood is usually fluid and dark red in color. Practically all the organs appear hyperemic, and small hemorrhages may be found in many of the organs, as well as in the pleurae, gastric and intestinal mucosa. In the cases which do not die rapidly, the signs noted are those of asphyxial death.

In the chronic type there may be hemorrhages in the skin, internal viscera, and of the serous surfaces. The blood is pale and watery, in contradistinction to that of the acute form of poisoning. There may be fatty degeneration of the heart muscle and liver. The bone marrow is aplastic, and may consist largely of fat[6], the few leucocytes present in stained sections being chiefly the so-called endothelial leucocytes (large mononuclears and transitionals).

Detection.—Benzene, toluene and xylene are largely eliminated from the body through the lungs, although small amounts are oxidized in the system and excreted in the urine, benzene in the form of phenol and conjugated sulphates and glycuronates, toluene in the form of hippuric acid, and xylene as toluric acid. It follows, therefore, that the urine may be examined for the presence of these oxidation products, but the amounts found will be small, although, of course, larger than under normal conditions.

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[1] Vrtljschr. f. gerichtl. Med., 1888, **49,** 138.

[2] Münch. med. Wchnschr., 1896, **43,** 915.

[3] U. S. Department of Interior, Bureau of Mines, Technical Paper 272, 1921.

[4] *Noxious Gases,* New York, 1927, p. 165.

[5] Jour. Amer. Med. Assoc., 1929, **93,** 1970.

[6] See Rohner, Baldridge and Hausmann, Arch. Path. and Lab. Med., 1926, **1,** 221.

In some of the cases reported, benzene was not detected in the tissues, probably because the methods employed were defective. Gettler[1], following his method of detection was able to isolate the following amounts of benzene per 100 grams of tissue: from the brain, 19.2 mg.; liver, 10.1 mg.; lung, 9.0 mg.; blood, 6.4 mg.; and heart, 2.4 mg. As benzene is relatively volatile, it is important that the tissues be kept cold while waiting to begin the analysis.

About 400 grams of tissue are ground up (preferably while in a frozen condition) and placed in a distilling flask. Add to this 400 cc. of water, thoroughly mix, and acidify with a few drops of sulphuric acid. Arrange the apparatus for distilling in steam, using a long condenser and allowing the outlet tube to dip into about 25 cc. of carbon tetrachloride. Distill for at least ½ hour, allowing a fast circulation of cold water to flow through the condenser. Place the distillate in a separatory funnel and shake for a few minutes. Allow the two layers of fluid to separate, draw off the lower layer of carbon tetrachloride, which contains most of the benzene, and place it in a clean, dry flask which is well stoppered. Now shake out the aqueous layer with fresh carbon tetrachloride three or four times, using, of course, fresh solvent each time and adding each successive portion of the solvent to the original extract in the flask. To this solution of the benzene in carbon tetrachloride add about 10 cc. of a 2:1 mixture of fuming nitric-sulphuric acid and shake thoroughly, to convert the benzene into the nitrobenzenes. Place the mixture in an evaporating dish and carefully evaporate the carbon tetrachloride on the water-bath. Allow the residue to cool, and treat it with about 50 cc. of water. Place the solution in a separatory funnel and extract several times with fresh portions of ether. Collect the ethereal portions and evaporate off the ether, when the nitrobenzenes are left as a yellow residue, which crystallize on standing. Weigh the residue, and from this calculate the amount of benzene present in the tissue. This residue may then be used for the following confirmatory qualitative tests.

1. Dissolve a portion of the nitrobenzene residue obtained as above in a few cc. of absolute alcohol, and make alkaline with a few drops of 30 per cent. sodium hydroxide solution. To this is added twice the volume of a 1 per cent. levulose (fructose) solution, when an intense violet color results, which gradually fades out.

2. Dissolve the remainder of the residue in about 10 cc. of water in a test-tube. Add about 2 grams of zinc dust and, then, concentrated hydrochloric acid drop by drop, until a fair reaction ensues. If the mixture gets too hot, cool it by immersing the tube in cold water. The nitrobenzene is reduced to aniline and phenyl diamine. Divide the solution into 2 parts, one consisting of about ⅓, and the remainder of two-thirds, and make the following tests. (*a*) To the smaller portion add

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[1] Jour. Pharm. and Exp. Therap., 1923, **21**, 161.

alcoholic sodium hydroxide solution to alkaline reaction, and follow this with a drop of chloroform. On warming slightly, the typical, disagreeable odor of phenyl-isocyanide is obtained. (*b*) To the larger portion of the reduced solution add a few drops of 10 per cent. sodium nitrite solution in order to form the diazo compound, then add sodium carbonate solution until the first precipitate of zinc carbonate forms, and follow this by the addition of about 3 cc. of 0.1 per cent. alkaline solution of beta-naphthol. An intense red-brown color is obtained[1].

Phenols

These aromatic compounds are derived from the hydrocarbons by replacement of one or more hydrogen atoms of the benzene ring by hydroxyl. The phenols are designated as mono-, di-, trihydric, etc., according to the number of hydroxyl groups entering the ring, all of the six hydrogen atoms being replaceable by hydroxyl. The phenols differ from the aromatic alcohols in that the hydrogen of the benzene ring is replaced by hydroxyl in the former, while in the latter the hydrogen of the side chains is replaced.

PHENOL (CARBOLIC ACID)

Carbolic acid forms the principal part of the "middle oil" passing over between 170° and 230°C., when coal tar is distilled. It is a product of animal metabolism and is found, therefore, in the urine of man in the form of conjugated sulphuric acid. It finds extensive use as an antiseptic and disinfectant, and is, as a result, very accessible to the general public. Since its introduction by Lister in 1863 as an antiseptic, it has given rise to numerous cases of poisoning, and is still much used as a suicidal poison, although less frequently than in past years. Although it is widely employed in industry, it rarely gives rise to industrial poisoning, as contact with it is kept down to a minimum and only occasional cases of splashing of the phenol on the body occur.

"In the registration area of the United States in 1909", say Hunt and Gettler[2], "1621 of the 3376 cases of death due to poison (in which the kind was specified) were due to phenol . . . There were 1740 deaths in England and Wales, 1901–18, due to phenol . . . The most frequent source of poisoning has been its use for suicidal purposes; it was the agent employed in 1466 of the 2372 cases in the United States in 1909 in which the poison was specified; of 1018 suicides by poison in England and Wales, 1912–13, phenol was employed in 152 cases. The next most frequent source of poisoning has been accidental; in the registration area of the United States in 1909 phenol was responsible for 155 of the 1004 cases of accidental death due to poisoning in which the kind of poison was specified." In New York City there were reported, from 1918 to 1920, 15 accidental and 47 suicidal cases of poisoning from carbolic acid, while in 1925–26 the number had fallen to 1 accidental case and 12 suicidal ones. In Chicago there were 47 cases of phenol poisoning from 1918 to 1920, of which 6 were accidental and 41 suicidal. Of 796 deaths from poisoning in St. Louis in 1910 to 1914, 506 were due to phenol, while, during the same period, it was responsible for 490 of the 692 cases of suicide by poisons. Homicidal cases are rare, although a few are found in the records[1].

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[1] See Hunt and Gettler, "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 693

[2] "Non-alkaloidal Organic Poisons," in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 701.

Carbolic acid poisoning has arisen from oral ingestion; from injection of the pure substance into the rectum, into abscesses, into the pleura, into the uterus, vagina, etc.; from absorption from wounds, burns, or from the intact skin; and even after application to the eye. Dilute solutions of phenol, especially, when applied to open wounds or injected into cavities, may cause serious poisoning; and even the application of dilute solutions to the intact skin, especially when the solution is prevented from evaporating by the use of impervious dressings, may cause both local disturbances, such as gangrene, and mild general symptoms. Witthaus states that "In 5 instances absorption has been by inhalation."

Properties.—Phenol (carbolic acid, benzophenol, phenic acid, C_6H_5-OH) occurs as colorless, interlaced, or separate needle-shaped crystals, or as a white or light pink, crystalline mass. It has a characteristic, somewhat aromatic odor, and a burning taste. The crystals melt at 41°C., and have a boiling point of 182°C. Phenol is soluble in about 15 parts of water at 25°C., and is very soluble in alcohol, glycerin, chloroform, ether, carbon disulphide, benzene, and in fixed or volatile oils, as well as in petrolatum or liquid petrolatum. When mixed with 10 parts of water, phenol is liquefied, forming the *Phenol liquefactum* of the Pharmacopoeia. The aqueous solution is neutral, or only faintly acid to litmus paper.

Symptoms.—Phenol produces both local and constitutional effects. It is a general protoplasmic poison, exerting its antiseptic action for this reason. It precipitates proteins, but, owing to the loose nature of this combination, the phenol easily penetrates the tissues causing severe burns and necrosis. This action is, therefore, that of a true corrosive. When applied locally to the skin, there is at first a tingling and numbness that may progress to almost complete anesthesia. If applied in concentrated form, the skin is blanched and, later, shows distinct burns, a white, opaque eschar forming, which may come off in a few days leaving a brown stain. If applied in the form of a dilute solution and prevented from evaporating by impervious dressings, dry gangrene of the part may result. Certain cases of eczema have been reported as resulting from the irritation caused by hat bands which have been treated with phenol[1], while the use of certain marker inks containing phenol have caused severe burns together with constitutional symptoms resulting from splashing of the fluid on the body[2]. It is probable that the external effects are a function not so much of the concentration of the phenol as of the time during which it remains in contact with the surface. It is of interest to note that combination of phenol with camphor results in the loss of the corrosive action.

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[1] See Witthaus, *Toxicology,* 1911, p. 1189; and Hofmann-Haberda, Lehrbuch der gerichtlichen Medizin, 11te. Aufl., 1927, p. 820.

When taken internally phenol causes a burning pain in the mouth and stomach. Vomiting may follow, but this is not always noted. Phenol is rapidly absorbed from the stomach and intestines, so that the constitutional symptoms come on quite soon. If large doses are taken, immediate unconsciousness may follow and death result in a few minutes, in some cases as rapidly as 10 minutes. This rapid death is, probably, the result of both the local corrosion with shock and collapse and of the action on the central nervous system. In the more gradual cases of poisoning, there are noted general depression and muscular weakness, headache, dizziness, pallor of the face, which is usually covered with a cold perspiration, excitement, mild delirium, noises in the ears, livid skin, weak, irregular, rapid pulse, irregular respiration, unconsciousness, and death. In some cases convulsions are noted, but these are relatively rarely seen, and occur somewhat more frequently in children than in adults. The breath may smell strongly of phenol, and the urine is usually dark in color (the color increasing on exposure of the urine to air) from the presence of conjugated sulphates and glycuronates of hydroquinol, pyrocatechol (oxidation products of phenol), conjugated and free phenol. The same train of symptoms is observed after absorption of phenol from whatever point it may be applied, although these appear somewhat more slowly than after oral ingestion.

Fatal Dose.—The lowest fatal dose of phenol has, probably, not been definitely settled. This will depend much on the method of administration and on the promptness with which treatment is instituted. Very small quantities of phenol cause death when introduced into wounds or into body cavities. Kobert[3] states that 1 gram may prove rapidly fatal under such circumstances, while Hunt and Gettler[4] regard 1 to 3 grams as a fatal dose when applied locally to wounds. In one case, reported by Edmund, a girl of 18 died in 1 hour and forty minutes after receiving a uterine douche containing 3.9 gram of phenol dissolved in a quart of water, even though much of the liquid was returned[5].

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[1] See Müller-Hess, Deutsch. med. Wchnschr., 1920, **46**, 491; and Schemel, Münch. med. Wchnschr., 1920, **67**, 700.

[2] McCord and Minster, Jour. Amer. Med. Assoc., 1924, **83**, 843.

[3] *Lehrbuch der Intoxikationen*, 2te. Aufl., 1906, **2**, 123.

[4] "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 703.

[5] Med. and Surg. Reporter, 1887, **57**, 345.

When phenol is taken internally, the fatal dose is larger than when it is absorbed from wounds or cavities. Although Falck regards the fatal dose as 15 grams, and Lewin states that this is 8.5 grams, there are many recorded cases of death from much smaller amounts. Thus, De Vries[1] reports the case of a girl found dead after having swallowed 1.5 gram of phenol in the form of a 3 per cent. solution; Anderson[2] reports the case of a man of 64 who died in 12 hours after having swallowed 3.9 grams of phenol in oily solution, while Wilkinson[3] cites a case of death of a girl of 17, who died in 23 hours from the same dosage. Recoveries have, however, occurred following such doses as 1 ounce, 1½ ounces, 2 ounces, and 4 ounces.

Fatal Period.—Death may result in a few minutes after the external use of phenol, or, in some cases, may be delayed for a few days. "In a large percentage of cases death occurs within one or two hours and it is not often delayed more than twelve hours. After very large doses death may occur with a few minutes."

Treatment.—The first indication is the removal of the phenol from the stomach by lavage, using 10 per cent. alcohol, warm water containing potassium permanganate, lime suspended in syrup, milk or white of egg. The lavage should be thorough after the use of any of these substances in the wash water, and should be done even if some time has elapsed since the phenol was ingested, as it has been shown that this poison remains in the stomach for some time. For the burns of the skin, use strong alcohol as a wash and apply oil dressings. In cases where the phenol has been introduced into cavities, as the vagina, rectum, or wounds, wash these out with dilute alcohol to remove the phenol and prevent its corrosive action. For the systemic effects, general measures should be adopted. Keep the body warm by hot packs in cases of collapse; administer intravenous saline infusions when circulatory depression is evident; for respiratory weakness artificial respiration must be employed.

Postmortem Appearances.—When phenol has been taken by mouth, there may be the white or brownish stains about the lips, angles of the mouth, or chin. The mucous membrane of the mouth, esophagus, stomach, and upper portions of the intestines may show areas of corrosion, which are white in color, and may be hardened, corrugated, and partly detached. In some cases the mucous membrane may be hyperemic, and show only a "spotty" necrosis. The blood is usually dark and fluid, although some of the large vessels may contain red thrombi. The odor of phenol may be marked in the different organs, or may be noticeable only in the stomach, while Cattell[4] in one of his cases observed the odor in the kidney but not in the stomach. The brain, meninges,

[1] Therap. Monatsch., 1890, **4**, 644.

[2] Lancet, 1869, **1**, 179.

[3] Therap. Gaz., 3 s., 1892, **8**, 220.

[4] Proc. Path. Soc., Phila., 1897, **1**, 19.

liver, spleen, lungs, and kidneys may show considerable congestion, while, in some cases, the liver may be fatty, the lungs may show edema, and the kidneys (in long-continued cases) evidences of hemorrhagic nephritis.

Detection.—Phenol may be recovered from the stomach contents, intestinal contents, the various organs, and the urine. In the detoxication of phenol by the system, the sulphuric acid formed by decomposition of the proteins is combined with the phenol, forming phenol-sulphuric acid, while part of the phenol is oxidized to pyrocatechol and hydroquinol, which combine with sulphuric and glycuronic acids and are excreted as conjugated acids. It happens, therefore, that the phenol in the system may exist largely in the form of conjugated compounds, and, partly, in the free state, this latter form being somewhat more significant. For this reason it is advisable always to make search for both types of phenol.

In the usual systematic examination for poisons, phenol is found in the distillate from acid solutions, but may, also, appear in the processes of extraction with ether or benzene. Pyrocatechol and hydroquinol are not volatile with steam. In carrying out the distillation process, it is wise to make a preliminary distillation of the material, especially of the stomach contents in cases in which the phenol has been swallowed, after very faintly acidifying with a weak acid such as acetic acid. Any phenol found here will have been originally present in the uncombined state. Should this distillate show the phenol reactions described below, a quantitative determination may be made by continuing such distillation until no further qualitative reactions obtain and by following the procedure outlined below for the determination. If no reactions are obtained for free phenol, or if the material has been distilled with weak acid until all free phenol is given off, thoroughly macerate the material with 5 per cent. sulphuric acid and distill with steam, when the combined phenol will be broken up and the phenol come over. If much phenol be present in the tissues, the first distillates may be cloudy and oily drops may float on the surface, the distillate having a noticeable odor of phenol. Small quantities usually remain dissolved in the aqueous distillate. In any case, the distillation is continued until a few drops of the distillate fail to give a reaction with bromine water. The distillate may then be purified by shaking it out with petroleum ether, which dissolves many impurities but does not dissolve appreciable amounts of phenol. After this purification, the aqueous distillate is shaken out with ether, which removes the phenol, as well as certain other derivatives, such as salicylic acid, which may give confusing reactions with the tests given below. If sodium carbonate solution be added to the original distillate, sodium salicylate forms, so that, on extracting with ether, the phenol passes into the ether, while the sodium salicylate is left behind. On allowing the ether to evaporate, phenol is obtained and may be tested for by the following tests. It is to be remembered that putrefaction of protein material may lead to the formation of traces of volatile (as well as non-volatile) compounds, some of them of the nature of phenol and p-cresol, which give the tests outlined below, so that conclusions must be guarded in the presence of marked putrefaction of the tissues.

1. *Millon's Test*[1].—To a little of the suspected distillate, or to an aqueous solution of the residue obtained as above described, add ½ its volume of Millon's reagent[2] and warm for a short time, when a light or dark red color will appear, depending on the amount of phenol present. This test is said to be sensitive to 1 part of phenol in 2 million of water, but it is by no means specific for phenol. It should, rather, be regarded as specific for monohydric phenols and their derivatives such as substitution products in which the hydrogen atoms of the benzene ring are replaced by hydrocarbon radicals, but not by substitution products in which the hydrogens are replaced by the halogens or carbon-free radicals. This reaction is given, also, by aniline and other primary, aromatic amines, but this is due to the fact that diazonium salts are first formed, which give rise to phenol on being warmed with water. With the polyhydric phenols, either a color other than red is produced, or the reagent is reduced with separation of mercury.

2. *Landolt's Bromine Water Test.*—To a few cc. of the distillate or to an aqueous solution of the suspected residue, add bromine water until the fluid remains permanently yellow. At once, or slowly if the amount of phenol be small, a yellowish-white crystalline (fine stars or needles) precipitate of tribromphenol ($C_6H_2Br_3OH$, 2-4-6-tribrom) separates. This tribromphenol dissolves readily in alcohol, ether, and alkalies but is insoluble in water and in acids. It melts at 96°C. The test is sensitive to 1 part of phenol in approximately 60,000 of water. If a large excess of bromine water is used, tribromphenyl hypobromite ($C_6H_2Br_4O$) forms, which melts at 131°C., and changes into tribromphenol by dissolving in alkalies and precipitating by acids. Other phenols, salicylic acid, and other substances give somewhat similar precipitates, but these differ in form of the crystals and in the melting point of the product.

3. *Liebermann's Test.*—Dissolve a small amount of the suspected residue in concentrated sulphuric acid and add a few drops of Liebermann's reagent[3], when intense colorations arise in the presence of the different phenols. With carbolic acid, the coloration is first brown, then green, and finally a deep blue. This blue solution becomes red upon addition of glacial acetic acid, or water, and turns blue again upon adding excess of ammonia.

4. *Eykmann's Test.*—This is really a modification of the above. To a portion of the distillate or an aqueous solution of the suspected residue,

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[1] C. R. Acad. des Sci., vol. 28, p. 40. This test is known, also, as Plugge's Test. See Plugge, Arch. der Pharm., 1890, 228, 9.

[2] Dissolve mercury in an equal weight of concentrated nitric acid, warming gently to start the reaction, and then dilute the product with twice its volume of distilled water. Allow to stand overnight, and decant the clear reagent.

[3] A solution of 0.6 gram of potassium nitrite in 10 grams of sulphuric acid.

add a few drops of an alcoholic solution of ethyl nitrite (*spiritus aetheris nitrosi*). Now underlay this mixture with concentrated sulphuric acid, when a rose-red ring forms at the zone of contact. This reaction is sensitive to 1 part in 2 million of water, but reacts with other substances, so that it is not specific.

5. *Deville's Ferric Chloride Test.*—To a few cc. of the distillate add very dilute ferric chloride solution, drop by drop, when a blue-violet or blue color is formed in the presence of phenol. This reaction is not a delicate one, and is given by many phenols and their derivatives, as well as by such non-phenolic compounds as antipyrine and pyramidon, although the shades of color obtained may vary somewhat with the different substance. With carbolic acid the presence of dilute mineral acids and of alcohol prevents the appearance of the color.

6. *Melzer's Benzaldehyde Test.*—To 1 cc. of the distillate add 2 cc. of concentrated sulphuric acid and 1 to 2 drops of benzaldehyde and heat just to the boiling point. In the presence of phenol, the liquid, which is yellowish-brown in the cold, becomes dark red in color, a red resinous substance separating unless the solution is too dilute. Allow this mixture to cool, pour this into 10 cc. of water, and make distinctly alkaline with potassium hydroxide. If phenol be present, a beautiful violet-blue color appears. This reaction is quite delicate, 1 cc. of a 0.5 per cent. solution of phenol giving a distinct blue color[1]. According to Gadamer[2], of the phenols that might come into question, o-cresol and phenol are the only ones giving this reaction, and the former does not give a permanent blue with ferric chloride, but a blue changing to green.

7. *Lex's Hypochlorite Test.*—To a few cc. of the distillate add about ¼ its volume of ammonium hydroxide, and then 2 to 4 drops of a freshly prepared solution of calcium or sodium hypochlorite. On warming this mixture, a beautiful blue color appears in the presence of phenol. If the solution is very dilute, only a green or a blue-green color is noted. With this test o- and m-cresol gives first a green and then a blue color, while p-cresol gives a dirty greenish color. Instead of using the hypochlorite, one may employ vapors of bromine.

Estimation.—Mix a weighed portion of the finely hashed tissue with some water, acidify with sulphuric acid so that the acidity of the mixture is about 5 per cent, and distill until the distillate shows no trace of turbidity with bromine water. Mix the distillate thoroughly and measure it exactly. Now transfer 25 cc. of this solution to a 500 cc. glass-stoppered flask with a long narrow neck. Add 25 to 50 cc. of N/10 bromine solution[3], depending upon the relative amount of phenol suspected, then

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[1] See Autenrieth, *Detection of Poisons,* 6th Amer. Ed., translated by Warren, 1928, p. 46.

[2] *Lehrbuch der chemischen Toxikologie,* 2te. Aufl., 1924, p. 318.

[3] Dissolve 3 grams of potassium bromate and 50 grams of potassium bromide in sufficient distilled water to make 1 liter. Determine the strength of this solution by titration with N/10 sodium thiosulphate after the addition of potassium iodide and a slight excess of hydrochloric acid, and adjust to exact normality.

5 cc. of concentrated hydrochloric acid, and insert the stopper at once. Shake the flask several times during ½ hour, allow it to stand for 15 minutes, remove the stopper just enough to allow the rapid introduction of 5 cc. of a 20 per cent. solution of potassium iodide without permitting bromine vapors to escape, and insert the stopper. Shake the flask thoroughly, remove the stopper and rinse it and the neck of the flask in such a way that the washings flow into the flask. Now add 1 cc. of chloroform, shake the mixture, and titrate with N/10 sodium thiosulphate solution, using starch solution as an indicator. Each cc. of sodium thiosulphate used to titrate the iodine liberated is equivalent to 1 cc. of N/10 iodine or of N/10 bromine solution. Hence, subtract the number of cc. of sodium thiosulphate used in the titration from the number of cc. of N/10 bromine originally added, and multiply this figure by 0.001568 gram to obtain the amount of phenol in the amount of distillate taken for examination. A simple calculation will then yield the total amount of phenol present in the tissue.

CRESOLS

The cresols are the next higher homologues of benzophenol, being the hydroxy derivatives of toluol. There are three possible isomeric cresols, the ortho-cresol, the meta-cresol, and the para-cresol. These, together with a small amount of phenol and aromatic hydrocarbons are the chief constituents of crude coal-tar creosote. The cresols, sometimes called cresylic acids, have been used in place of carbolic acid as antiseptics, and are readily accessible to the public in the form of various proprietary products, such as lysol, creolin, solveol, solutol, saprol, and trikresol. The cresols are all poisonous, the meta form being less toxic and less irritant to mammals than is phenol, although it appears to have more powerful antiseptic properties; the ortho compound is more toxic than is phenol; while the para derivative is the most poisonous of the three[1]. The toxicity of the combined cresols (trikresol) is, according to Hale[2], about 0.9 of that of phenol. The toxicity of the cresols is diminished by replacing the hydrogen of the hydroxyl group by acid radicals.

Owing to the ease with which various preparations of cresol may be obtained, it is not surprising to find that there have been a large number of cases of poisoning traceable to these different phenolic compounds. Practically all of the preparations of cresol have figured in the reports of poisoning, although lysol is, probably, the agent most frequently used. According to Hunt and Gettler[3], 277 cases of lysol poisoning with 81 deaths were treated in two Berlin hospitals in the years 1904 and 1905. Blumenthal[4] estimates that more than 100 cases of lysol poisoning occur annually in Berlin, while Friedländer[1] raises this figure to at least 200 cases. Feldman[2] states that of all poisonings, suicidal and accidental, occurring in Hamburg from 1904 to 1908, those by lysol took the first place, while Sieveking[3] reports that lysol was taken with suicidal intent by 425 persons in Hamburg between 1904 and 1917. Although large numbers of cases of poisoning by carbolic acid occurred in England in the years preceding 1900, the number has markedly diminished in recent years, the report of the Registrar-General for 1918 showing only 29 cases of poisoning from carbolic acid and 4 from lysol. The reports of the Chief Medical Examiner of New York City show 40 suicidal and 4 accidental lysol deaths in 1925, and 30 suicidal and 10 accidental cases in 1926. The reports of the Coroner's Office of Cook County, Illinois, for the years 1918 to 1920 show 11 accidental, 7 suicidal, and 1 homicidal deaths from lysol. Witthaus[4] has collated the reports of 133 lysol poisonings up to 1911, of which 13 were by external application, with 3 deaths; 11 by uterine irrigation, with 5 deaths; 107 by internal administration, of which 23 were accidental, with 7 deaths, 84 suicidal, with 21 deaths, and 2 homicidal, with 1 death.

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[1] See Wandel, Arch. f. exp. Path. u. Pharm., 1907, **56**, 161.

[2] Bull. 88, Hyg., Lab., U. S. Public Health Service, 1913. See Smith, Brit. Med. Jour., 1928, **1**, 714 for a fatal case of poisoning with cresylic acid.

[3] "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 711.

[4] Deutsch. med. Wchnschr., 1906, **32**, 1283.

Witthaus, also, cites the reports of 12 cases of creolin poisoning, of which 9 were accidental, with 1 death, and 3 suicidal, with 1 death, while 11 fatal cases of creolin poisoning occurred in Prussia from 1906 to 1912[5]. Dost[6] reports a fatal suicidal poisoning by saprol.

Properties.—Cresol (U. S. P.) is a mixture of the 3 isomeric cresols ($C_6H_4CH_3OH$) obtained from coal tar. This is a colorless, or yellowish to brown-yellow, or a pinkish, highly refractive liquid, becoming darker with age and on exposure to light. It has a phenol-like odor, and has a specific gravity ranging from 1030 to 1038 at 25°C. Of the three cresols, the ortho compound melts at 30.1°C. and has a boiling point of 190.8°C; the meta form melts at 10°C. and boils at 202.8°C.; while the para derivative melts at 34.8°C. and boils at 201.1°C. Not less than 90 per cent. of the official cresol distils between 195° and 205°C. One cc. of cresol is soluble in about 50 cc. of water, usually forming a cloudy solution. It is miscible with alcohol, ether, benzene, petroleum benzin, and with glycerin, and is dissolved by solutions of the fixed alkali hydroxides.

The official *Liquor Cresolis Compositus* is a clear, brown, oily liquid prepared by treating cresol with linseed oil and solution of potassium and sodium hydroxides and heating to about 70°C. until it gives a clear solution when mixed with 9 volumes of cold water. This is very similar to the preparation "lysol", which is widely used by the public as an antiseptic and which has caused many poisonings. Creolin (Pearson)

[1] Therap. Monatschr., 1908, **22**, 536.

[2] Münch. med. Wchnschr., 1908, **55**, **26**.

[3] Vrtljschr. f. ger. Med., 1918, **56**, 163.

[4] *Toxicology*, 1911, p. 1187.

[5] Das Gesundheitswesen im Preuss. Staat., 1905–1912 (cited by Hunt and Gettler).

[6] Arch. f. krim. Anthrop., 1903, **10**, 96.

is a dark-brown, syrupy liquid with a tar-like odor, and consists of cresols held in suspension with rosin soaps. This creolin is said to contain about 12.7 per cent. cresols, while lysol contains approximately 50 per cent. of these phenolic compounds.

Symptoms.—The cresols cause both local and constitutional symptoms. Owing to the strong alkaline character of the preparations of lysol, the symptoms noted are, in reality, a combination of those of the alkali with that of the cresols. There is, therefore, somewhat more corrosive action than with carbolic acid, the mouth, throat, and stomach especially showing this effect. There is, often, vomiting of a brownish, bloody material, which arises from the gastric irritation, while the abdominal pain is usually more marked than with the ordinary phenol. The general constitutional symptoms are practically the same as given under phenol, although there may be more marked evidence of damage to the lungs, liver, and kidney than that following the ingestion of phenol.

The ortho and para cresols are more easily oxidized in the system, than is the meta compound, the former appearing as conjugated sulphuric and glycuronic acid compounds of the oxidation products (paraoxybenzoic acid, pyrocatechol, and hydroquinol), while the latter is apparently directly combined with the conjugating acids.

Fatal Dose and Period.—Death has resulted, both in the case of an adult and a child, from a dosage of 1 to 2 teaspoonfuls (4 to 8 cc.)[1], while other cases have resulted fatally following doses of a tablespoonful (15 cc.)[2] of lysol. Recovery has occurred following such doses as 50 cc., 90 cc., 100 cc. and more. In regard to the fatal dose of creolin Witthaus states that "we find no record of its having caused death when taken *per os*, although in two cases 250 grams (8 oz.) were swallowed by suicides who recovered.

As the cresols are absorbed somewhat more slowly than is phenol, we find that death does not occur so rapidly after their use. Thus we find that death of an adult resulted in Weissenrieder's case in hour, while in that reported by Raede a child of 10 months did not die for 36 hours, both cases having ingested 4 cc. of lysol. Birnbaum[3] reports the death of a woman of 29 in 30 minutes after an irrigation with ½ per cent. solution of lysol following an extraperitoneal Cesarean section.

Treatment.—The treatment of cresol poisoning is practically the same as that of phenol poisoning. On account of the stronger corrosive action of the cresols, there is danger of edema of the glottis, which may need special attention.

Postmortem Appearances.—The marks of corrosion about the lips and the angles of the mouth are rarely absent in cresol poisoning. So, also, we may find more evidence of corrosion in the throat, esophagus, and stomach than in cases of phenol poisoning. The changes in the liver seem to be more severe and more frequent than those in phenol poisoning, the pathologic picture being variable, some cases showing parenchymatous hepatitis, some yellow atrophy, and others simple thrombosis of the vessels.

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[1] See Weissenrieder, Med. Corr.-Bl. d. Würt, A.-Verein, 1909, **79**, 437; and Raede, Deutsch. Ztschr. f. Chir., 1893, **36**, 565 (both cited by Witthaus).

[2] See Dost, Arch. f. krim. Anthrop., 1905, **18**, 95; and Ebhardt, Ztschr. f. Med.-Beamte, 1901, **14**, 495.

[3] Centralbl. f. Gynec., 1909, **33**, 1521.

Detection.—The isolation of the cresols is accomplished in the same manner as that of phenol, namely, by distilling the strongly acid tissues with steam. If the distillate be shaken with ether, the cresols, as well as hydrocarbons are extracted. Allow the ether to evaporate, take up the residue with dilute sodium hydroxide solution and shake out with petroleum ether, which will remove the hydrocarbons. On now acidifying the alkaline aqueous solution with dilute hydrochloric acid and extracting with ether, the cresols are extracted. Allow the ether to evaporate, take up the residue with a little water and perform the tests outlined under phenol. The cresols give a positive Millon's test and ferric chloride test. The colorations of the cresols with ferric chloride are slightly different from that given by phenol, and are, also, slightly different for each cresol. Thus, o-cresol gives a blue changing shortly to green; m-cresol shows an evanescent blue changing to a dirty yellowish-brown; while p-cresol strikes a permanent blue-violet. Only o-cresol shows a positive benzaldehyde reaction, while with Lex's test o- and m-cresol give first a green and then a blue color, and p-cresol produces only a dirty greenish color.

CREOSOTE

Under this term are included two distinct chemical compounds. The coal-tar creosote is the so-called "heavy oil" obtained from coal tar and distilling between 230° and 270°C. This consists of a mixture of phenol, cresol, and aromatic hydrocarbons, especially anthracene. The product of distillation of wood-tar is known as creosote and contains no free phenol or cresol, but is a mixture of phenols, chiefly guaiacol (C_6H_4-$OHOCH_3$, methyl pyrocatechol) and creosol ($C_6H_3CH_3OCH_3OH$, methyl homopyrocatechol), with small amounts of phloral (methyl creosol). The official creosote is, usually, obtained from beech wood-tar.

Poisonings from creosote, or from its most important constituent, guaiacol, are not as numerous as those from the cresols, but quite a number have been reported in the literature. Witthaus[1] cites 19 cases of creosote poisoning, of which 11 were accidental, with 5 deaths, 1 a successful suicide, 4 successful homicides, 1 an attempted abortion, and 2 of uncertain origin. Of the 11 accidental cases, 3 resulted from mistakes in its medicinal administration, 3 from accidents consequent upon its use for relief of toothache, 3 from its medicinal use internally, 1 from a pharmacist's error, and 1 by mistake for brandy. At least two fatal accidental poisonings from guaiacol have been reported[1], one of these being from internal administration, and one from its external application.

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[1] *Toxicology*, 1911, p. 1188.

Properties.—The official creosote is "an almost colorless or yellowish, highly refractive, oily liquid, having a penetrating, smoky odor, and a burning, caustic taste." It is slightly soluble in water, but is miscible with alcohol, ether, and with fixed or volatile oils. It has a specific gravity not below 1.076 at 25°C. Not less than 90 per cent. of it distills between 200° and 220°C. When mixed with equal parts of collodion, no permanent coagulum is produced, while phenol and the so-called coal-tar creosote coagulates the collodion at once.

Creosote Carbonate (U.S.P.) is a mixture of the carbonates of the various constituents of creosote. It is a clear, colorless or yellowish, viscid liquid, odorless and tasteless, or may have a slight odor and taste of creosote. It is insoluble in water, but is freely soluble in alcohol, petroleum benzine and in fixed oils, and is miscible with chloroform and benzene.

Guaiacol is official and occurs either as a liquid or a solid. Liquid guaiacol is colorless or yellowish, while solid guaiacol is crystalline, and is colorless or yellowish. One gram of guaiacol is soluble in from 60 to 70 cc. of water and in 1 cc. of glycerin at 25°C. It is miscible with alcohol, chloroform, ether, and with glacial acetic acid. Guaiacol melts at 28°C. and boils at 205.1°C.

The official guaiacol carbonate ($(C_6H_4OCH_3O)_2CO$) occurs as small, colorless crystals, or a white, crystalline powder. It is odorless and tasteless, or has a slight aromatic odor and taste. It is insoluble in water. One gram is soluble in 60 cc. of alcohol, 1 cc. of chloroform, and in 18 cc. of ether at 25°C. It is freely soluble in boiling alcohol and benzene, and is slightly soluble in glycerin and in fixed oils. It melts between 85° and 88°C.

Symptoms.—Practically the same as those following phenol poisoning. The breath may smell strongly of creosote.

Detection.—Creosote and guaiacol are both volatile with steam. The distillate is treated in the same way as discussed under cresols. A strong aqueous solution of the residue from the ether extraction of the distillate shows the following reactions, most of them being discussed under phenols.

Millon's and Eykmann's tests give red colors. Addition of ferric chloride gives a transient violet-blue or blue-gray color, which changes rapidly to a gray-green and then a muddy brown, the liquid becoming cloudy, if creosote or guaiacol be present. (If an alcoholic solution of guaiacol be treated with ferric chloride, color is produced, changing to emerald-green, and finally becoming yellowish.) Bromine water produces a deep orange brown changing to coffee brown precipitate of tribromguaiacol. With Liebermann's test a beautiful, deep violet color is produced. If the aqueous solution is treated with 1 cc. of chloroform, a piece of potassium hydroxide added, and the mixture warmed to about 60°C., a red color is obtained. For a detailed discussion of the examination of the urine in a case of creosote poisoning see Boruttau and Stadelmann[1].

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[1] Wyss, Deutsch. med. Wchnschr., 1894, **20**, 296 and 321; and Lewin, *Lehrbuch der Toxikologie*, 1897, p. 216.

Pyrogallol

Of the three trihydric phenols, pyrogallol, phloroglucin, and oxyhydroquinol, the first is, probably, the most important toxicologically. It is a very strong reducing agent, its alkaline solution absorbing oxygen very energetically, for which reason it finds wide use in gas analysis for the determination of oxygen, and, also, is frequently employed in bacteriology in furnishing an oxygen-free atmosphere for the development of anaerobic organisms. Further, commercial uses of this compound are found in the dye and photographic industries. Medicinally it has found somewhat frequent employment in the treatment of certain skin diseases, especially psoriasis.

Pyrogallol has caused poisoning from absorption through the skin, and, also, after internal administration. Although not introduced as a therapeutic agent until 1878 by Jarisch, it was not long until a case of poisoning from its external use was recognized, Neisser[2] reporting such a case in 1880. Witthaus[3] cites 13 cases of pyrogallol poisoning, 6 by external, medicinal application, with 2 deaths, and 7 by internal administration, of which 3 were suicidal, with 3 deaths. At least three recent fatal cases[4] must be added to the above number.

Properties.—Pyrogallol (v-Trihydroxybenzene, $C_6H_3(OH)_3$) is a light, white, or nearly white, odorless crystalline powder, occurring as leaflets or fine needles. It may acquire a grayish tint on exposure to air and light. It melts at 134° and boils at 309°C. One gram is soluble in 1.7 cc. of water, in 1.3 cc. of alcohol, and in 1.6 cc. of ether at 25°C. It is very soluble in boiling water and in boiling alcohol. It is difficultly soluble in chloroform, benzene and carbon disulphide. Its alkaline solution absorbs oxygen very energetically, turning brown, and decomposing into carbon dioxide, acetic acid, and brown substances.

Symptoms.—Pyrogallol acts rapidly and markedly upon the blood-corpuscles, producing a very great degree of methemoglobinemia. The red corpuscles lose their color and become shrunken, many so-called "ghost" cells being noticed microscopically. The hemoglobin passes out of the cell and is converted into methemoglobin, the blood becoming reddish-brown in color. As a result of these changes, there is a reduction in the oxygen-carrying power of the blood, so that symptoms of anoxemia may be observed. Secondary symptoms of icterus, methemoglobinuria, hemoglobinuria, and signs of a gradually progressing nephritis appear. As symptoms of this condition of affairs, one notes headache, chills, vomiting, diarrhea, marked cyanosis, pulse small and weak. There may be febrile reactions in some cases, while in others the temperature may be subnormal. The urine becomes dark in color, contains albumin, hemoglobin, casts, and, often, red blood cells. The cyanosis may increase, tremors may develop, although convulsions are rare, and death occur in a state of collapse. In some cases death may be due to embolism arising from the degenerated, shrunken red cells. In some cases, the gradually progressing nephritis may lead to a high degree of nitrogen retention, anuria, and, ultimately, to fatal uremia. In some cases there may be a toxic erythematous eruption, which is more or less generalized, and bleeding from various mucous membranes may obtain. In a recent fatal case occurring in the Albert Merritt Billings Hospital of the University of Chicago[1], which resulted from the ingestion of about 20 grams of pyrogallol and in which death did not occur until the 20th day of the poisoning, the chief features of the case in the order of their appearance were as follows. Nausea, vomiting, diarrhea, ashy-gray cyanosis with icterus, methemoglobinemia and hemoglobinemia, hemoglobinuria, fever, leucocytosis, anuria, oliguria, toxic erythema, nitrogen retention, ulcerative stomatitis and pharyngitis, generalized sub-mucous hemorrhages, coma, collapse, and death.

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[1] Deutsch. Arch. f. klin. Med., 1907, **91,** 42.

[2] Ztschr. f. klin. Med., 1880, **1,** 88.

[3] *Toxicology,* 1911, p. 1188.

[4] See Pewny, Med. Klinik, 1925, **21,** 970; and Kislitschenko, Ibid., 1926, **22,** 1341; unreported case occurring at Albert Merritt Billings Hospital, Chicago, (1929).

Fatal Dose and Period.—The fatal dose of pyrogallol is uncertain. In one case, according to Hunt and Gettler,[2] 75 grains (4.88 grams) contained in about 3½ ounces (108.8 grams) of salve were said to have been fatal. In a case reported by Dalché[3] a male suicide of 23 died after taking 15 grams, while Reilly[4] cites a case of a female suicide of 32, who died in 68 hours after swallowing 30 grams. In the case cited above as occurring in the Billings Hospital in Chicago, 20 grams were ingested, part of which was lost by vomiting, and death resulted on the 20th day. Smith[5] reports a case of death in 5 days following the drinking of an alcoholic liquid containing 250 grains (16.25 grams). Witthaus[6] states that no recovery has been reported from larger doses than 15 to 30 grams, "the maximum recovered from having been 8 gm. (124 gr.), taken along with 0.25 gm. (3.8 gr.) of pilocarpine in Maillart and Audeoud's[7] case." Death occurred in 24 hours following the application of pyrogallol salve to ⅔ of the body surface[8].

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[1] I am indebted to Dr. Emmet B. Bay of the University of Chicago for a history of this case.

[2] "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 710.

[3] Semaine med., 1896, **16**, 211.

[4] Brit. Med. Jour., 1897, **2**, 81.

[5] Pacific Med. Jour., 1891, **34**, 456.

[6] *Toxicology*, 1911, p. 1195.

[7] Rev. méd. de la Suisse Rom., 1891, **11**, 552.

[8] Pewny, Med. Klin., 1925, **21**, 970.

Treatment.—The application of the pyrogallol to the skin should be removed at once, or, if the poison has been ingested, the stomach should be promptly washed out with warm water. Multiple venesections, followed by transfusions, should be persisted in and begun as early as possible. Inhalation of oxygen may be of some value, although the indications for its use are rather infrequent in these cases. For the severe renal lesions, decapsulation of the kidneys may be of value.

Postmortem Appearances.—If the pyrogallol has been used locally, the skin is usually colored dark at the point of application. In the cases which run a somewhat rapid course, there is jaundice, but this may disappear should the case be prolonged for a week or more. In Neisser's case the cardiac ventricles contained reddish-brown coagula, as did the large vessels. The kidneys are enlarged and may appear almost black, showing, macroscopically and microscopically, evidences of inflammatory processes. The pelvis of the kidneys, the ureters, and the urinary bladder may contain considerable bloody fluid. In the prolonged cases, there may be extensive hemorrhage into the alimentary canal, and acute necrotizing stomatitis, pharyngitis, and esophagitis may obtain. The lungs may show edema, or areas of bronchopneumonia may be noted, possibly as terminal conditions.

Detection.—Pyrogallol belongs to the group of polyhydric phenols, which are not volatile with steam. It can not, therefore, be isolated by distillation, but must be separated by extraction methods. Extract the tissues with hot water made slightly acid with sulphuric acid. Filter and shake out this filtrate with benzene to remove fat. After withdrawal of the benzene layer, extract the acid aqueous solution with ether, repeating this extraction several times. On separating the ether layer and allowing this to evaporate, the pyrogallol is left in the residue, and may be identified by its physical properties as mentioned above and by the following tests.

If some of the residue be dissolved in a little water and allowed to stand in the air for some time, the color gradually changes to brown. If the original aqueous solution be rendered alkaline with sodium hydroxide, the solution becomes first violet, changing rapidly to brown, and then becomes black.

With Millon's reagent[1], pyrogallol gives no red color, but reduces the reagent to metallic mercury. It reduces, also, solutions of silver or gold salts to the metallic form. With Eykmann's reaction it gives a reddish-brown ring, while Liebermann's reagent produces a brownish-black coloration. Ferric chloride solution produces a red color, which becomes bluish on addition of a little calcium carbonate. Ferrous sulphate gives a blue-black coloration. An iodine solution imparts a purple-red color to either the aqueous or alcoholic solution.

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[1] For the composition of the reagents mentioned in this paragraph, see pages 798 and 799.

SALICYLIC ACID AND DERIVATIVES

Salicylic acid is found in the free state in some species of the violet, and occurs in the form of the methyl ester in *Spiraea ulmaria* (meadowsweet, queen of the meadows), in the leaves of *Gaultheria procumbens* (wintergreen), and in the bark of *Betula lenta* (birch bark). As salicylic acid has been shown to possess certain effects in inhibiting fermentation and putrefaction, it has been used, from time to time, as an agent for preserving foods and beverages, but such use is largely prohibited at the present time. Technically it has been widely employed in the manufacture of various dyes, and, medicinally it and its salts and esters have found wide application in the treatment of rheumatic conditions, and, also, in controlling fevers and certain types of headache.

While the number of cases of poisoning by salicylic acid and its derivatives is not as large as that reported for many other benzene compounds, yet sufficient cases have occurred to warrant the statement that salicylic acid should be used with some caution. Poisoning with salicylic acid itself, or with its salts, especially sodium salicylate, have resulted from the medicinal use of such compounds in treatment of rheumatic fever. Death has resulted from its absorption from the skin, as well as from internal administration[1]. Methyl salicylate has, apparently, caused more poisonings than salicylic acid or its salts, judging from the reported cases. According to Wetzel and Nourse[2], there are in the literature 11 cases of methyl salicylate poisoning (up to 1926), of which 5 were fatal. To these must be added the case reported by Wetzel and Nourse, the fatal case of Pincus and Hadley[3], the two fatal cases reported by Woodbury and Nicholls[4], the fatal case of Arnold and Jacobsen[5], and the two non-fatal cases of Olmsted and Aldrich[6]. Although it might be expected that phenyl salicylate (salol) might lead to many cases of poisoning, owing to its decomposition into salicylic and carbolic acids, yet few cases seem to have found their way into the literature[7]. Acetylsalicylic acid has lead to a few cases of poisoning, which are usually the result of therapeutic overdoses, although at least 5 fatal suicidal cases have occurred in Budapest alone. Most of the reported cases have been characterized by acidosis, as is the case in poisoning with methyl salicylate, but some have shown nothing characteristic, so that differentiation from salicylic acid poisoning must rest on the chemical examination[1].

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[1] See Quincke, Berl. klin. Wchnschr., 1882, **19**, 709; Langmead, Lancet, 1906, **1**, 1822; Miller, Jour. Amer. Med. Assoc., 1914, **63**, 1107; Zumbroich, Monatsschr. f. Kinderhkde., 1918, **15**, 167; Meyer, Arch. f. Kinderhkde., 1926, **78**, 269: Jørgensen, Ugeskrift f. Laeger, 1928, **90**, 31.

[2] Arch. Path. and Lab. Med., 1926, **1**, 182.

[3] Bull. Johns Hopk. Hosp., 1927, **41**, 163.

[4] Canad. Med. Assoc. Jour., 1928, **18**, 167.

[5] Bull. Buffalo Gen. Hosp., 1927, **5**, 44.

[6] Jour. Amer. Med. Assoc., 1928, **90**, 1438.

[7] See Hesselbach, Fortschr. der Med., 1890, **8**, 453; and Chalpowski, Therap. Monatsh., 1891, **5**, 213.

Properties.—*Salicylic acid* (o-hydroxy benzoic acid, $C_6H_4OHCOOH$) occurs in the form of a fine white needles, or a bulky, crystalline, white powder, or, when prepared from natural methyl salicylate, may have a slightly yellow or pink tint. It has a sweetish, afterwards acrid taste. It melts between 157° and 159°C. It is soluble in 460 parts of water, 2.7 parts of alcohol, 42 parts of chloroform, 3 parts of ether, 3 parts of acetone, 135 parts of benzene, and 52 parts of oil of turpentine at 25°C., and in about 15 parts of boiling water. Besides the official *Acidum Salicylicum*, the following salts are official: Ammonium salicylate, Bismuth subsalicylate, Eserine salicylate, Mercuric salicylate, Sodium salicylate, and Strontium salicylate.

Methyl Salicylate (oil of gaultheria, oil of wintergreen, oil of betula, oil of sweet birch, oil of teaberry, $C_6H_4OHCOOCH_3$).—This is produced synthetically or is obtained by distillation of the leaves of *Gaultheria procumbens*, or from the bark of *Betula lenta*. It is a colorless, yellowish, or reddish liquid, having the characteristic odor and taste of wintergreen. The specific gravity of the synthetic compound ranges from 1.180 to 1.185 at 25°C., while that derived from gaultheria or betula is from 1.176 to 1.182. It boils between 219° and 224°C. The synthetic methyl salicylate, as well as that derived from betula, is optically inactive, while that derived from gaultheria is slightly levorotatory. Methyl salicylate is slightly soluble in water, but is miscible with alcohol and with glacial acetic acid. It is soluble in about 7 volumes of 70 per cent. alcohol at 25°C. An alcoholic solution is neutral or slightly acid to moistened litmus paper.

Phenyl Salicylate (salol, $C_6H_4OHCOOC_6H_5$) is a white, crystalline powder, having an aromatic odor, and a characteristic taste. It melts between 41° and 43°C. It is very insoluble in water (1 part in 6670 cc.), but readily soluble in alcohol, chloroform, ether, benzene, and in fixed or volatile oils.

Acetylsalicylic acid (aspirin, $C_6H_4O(CH_3CO)COOH$) occurs as small, colorless crystals or needles, or a white crystalline powder. It is odorless, but has a sour taste. It melts at a temperature not below 132°C. It is readily decomposed by warming with water into salicylic and acetic acids. It is soluble in about 300 parts of water, 5 parts of alcohol, 17 parts of chloroform, and in from 10 to 15 parts of ether at 25°C. It is soluble with decomposition in solutions of alkali hydroxides and carbonates.

Symptoms.—When applied locally to wounds, mucous membranes, or even to the intact skin, salicylic acid may cause some corrosion and necrosis. It is this action that has lead to the frequent use of salicylic acid preparations in the removal of corns. When taken internally in the form of the powder, it may cause irritation of the mouth, throat, esophagus, and stomach, the mucous membrane of the latter not infrequently showing severe corrosion in some fatal cases. Dilute solutions of the acid and its derivatives may produce pain and discomfort, even nausea and vomiting, when ingested.

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[1] See Hansen, Ugeskrift f. Laeger, 1924, **86**, 249; Bucharest Letter, Jour. Amer. Med. Assoc., 1924, **83**, 1522; de Jankovich, Ann. méd. lég. criminol. et de police sci., 1928, **8**, 7; Hultkvist, Acta Med. Scand., 1929, **71**, 165.

Individuals differ markedly in their reaction to the effects of salicylic acid derivatives, some being hypersensitive to such an extent that small doses may produce serious symptoms. Although these compounds are rapidly absorbed from the intestine, large doses are required to produce toxic effects, except in those showing an idiosyncrasy. The symptoms of mild poisoning, or, probably, speaking more accurately, the symptoms of therapeutic limit of dosage, are nausea, vomiting, occasionally diarrhea, a feeling of fulness in the head, ringing or roaring in the ears, dimness of vision, profuse perspiration, confusion, and dulness. If the drug is still persisted in at this time, or if larger doses are initially taken, there may be noted flushing of the face, dyspnea, characterized by deep and labored respiration, slow, weak pulse, subnormal temperature, convulsions, coma, collapse, and death. In some cases delirium and hallucinations of sight and hearing may be observed, these being more frequently seen in chronic alcoholics and in diabetics than under other conditions according to Cushny[1]. Hemorrhages from the mouth, nose, stomach, intestine, or uterus may be observed, and various types of skin eruptions may appear following repeated doses of these salicylic acid derivatives, or, even, after single doses. Occasionally, especially in poisoning with acetylsalicylic acid, edemas, possibly of the angioneurotic type, may be seen[2]. Signs of nephritis may appear[3], the urine containing albumin, casts, and blood, and, especially in poisoning with phenyl salicylate, assuming the same dark olive-green color noted in phenol poisoning. In both methyl salicylate and acetylsalicylic acid poisoning quite a marked acidosis has been reported[4], a finding which at least is not commonly reported in cases of direct salicylic acid poisoning. In cases of poisoning with phenyl salicylate, the train of symptoms may be a mixture of those of both salicylic acid and phenol, but, occasionally, the symptoms noted more closely resemble those of phenol alone.

Fatal Dose and Period.—Owing to the difference in susceptibility of individuals to the action of salicylic acid and its derivatives, we find some fatal cases arising from relatively small doses, while other cases have recovered after intake of very large doses. Thus, Kobert[5] mentions a case fatal in 40 hours after ingestion of 3 grams, and Hunt and Gettler[1] state that "Death has, however, been attributed to doses of 4, 5, and 10 grams." These figures are, probably, too low for the average fatal dose of salicylic acid, and may, possibly, be attributed either to idiosyncrasy or to toxic impurities in the drug used. Hanzlik[2], in a study of the toxicity of different salicylates in adult males and females, respectively, found the *toxic* dose to be as follows: 180 and 140 grains of the synthetic salicylates; 200 and 135 grains of the natural sodium salicylate; 120 minims of the methyl salicylate; 165 and 120 grains of acetyl salicylate; and 100 and 83 grains of salicylo-salicylic acid. Cases of death have been reported from the application of a 10 per cent. salicylic acid ointment to the head and neck of an infant[3], while Quincke[4] reports death of a 17 year old patient from intake of 34 grams of sodium salicylate, and Langmead[5] the death of a child of 5 from 100 grams of the same drug. Cases of death from methyl salicylate have been reported from doses of 10 cc. taken by a child of 21 months[6], 12 cc. by a child of 3 years[7], 30 cc. by a woman of 25 years[8], while other fatal cases have followed the ingestion of 45[9] and 60[10] cc. Intake of 1 gram[11] and of 8 grams[12] of salol have proven fatal, while fatal results have followed the intake of 20 grams of acetylsalicylic acid[13]. In practically all the cases mentioned above, the subjects were receiving treatment for disease, so that it is difficult to state that the fatal outcome was due, in all cases, to the dosage mentioned.

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[1] *Text-Book of Pharmacology and Therapeutics*, 9th ed., edited by Edmunds and Gunn. 1928, p. 524.

[2] See Morgan, Brit. Med. Jour., 1911, **1**, 307; Brown, Lancet, 1911, **2**, 761; Macht, Med. Rec., 1911, **80**, 826; Graham, Jour. Amer. Med. Assoc., 1911, **56**, 261; Shelby, Ibid., 1918, **71**, 1381; and Kitchin, Ibid., 1920, **74**, 880.

[3] See Hanzlik, Scott and Thoburn, Arch. Int. Med., 1917, **19**, 1029; 1917, **20**, 329.

[4] See Olmsted and Aldrich, Jour. Amer. Med. Assoc., 1928, **90**, 1438; and de Jankovich, Ann. de méd. lég. de criminol. et de police sci., 1928, **8**, 7.

[5] *Lehrbuch der Intoxikationen*, 2te. Aufl., 1906, **2**, 136.

Treatment.—Where toxic symptoms have appeared following therapeutic use of the salicylates, withdrawal of the drug will, usually, be followed by more or less prompt disappearance of these symptoms. Where serious poisoning has occurred, gastric lavage with warm dilute (1 per cent.) sodium bicarbonate solution should be promptly carried out. Demulcent drinks should then be given to relieve the irritation of the gastric mucosa. Measures should be taken to increase the elimination of the drug through the kidney. In cases in which there are signs of renal insufficiency, attempts to stimulate renal activity may be attended with some danger. As has been shown[14], even therapeutic doses of the salicylates may lead to some renal involvement, as shown by the appearance of albumin and casts in the urine, the simultaneous administration of bicarbonates having little or no effect on the albuminuria. In such cases, therefore, copious draughts of water would seem to be the most acceptable method of increasing the renal elimination. In poisoning with methyl salicylate and acetylsalicylic acid, in which acidosis is quite a prominent symptom, bicarbonates should be given until the urine becomes alkaline.

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[1] "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 716.

[2] *The Salicylates.* Annual Report for 1914 for the Therapeutic Research Committee of the Council on Pharmacy and Chemistry of the Amer. Med. Assoc.

[3] Zumbroich. Monatssch. f. Kinderhkde., 1918, **15**, 167.

[4] Berl. klin. Wchnschr., 1882, **19**, 709.

[5] Lancet, 1906, **1**, 1822.

[6] Wetzel and Nourse, Arch. Path. and Lab. Med., 1926, **1**, 182.

[7] McNerthney, Northwest Med., 1903, **1**, 495.

[8] Pinkham, Boston Med. & Surg. Jour., 1887, **117**, 548.

[9] Jewett, New York Med. Gaz., 1867, **1**, 380.

[10] Legrain and Badonnel, Paris Letter, Jour. Amer. Med. Assoc., 1922, **78**, 1140.

[11] Chalpowski, Therap. Monatsch., 1891, **5**, 213.

[12] Hesselbach, Fortschr. der Med., 1890, **8**, 453.

[13] See de Jankovich, Ann. méd. lég. de criminol. et de police sci., 1928, **8**, 7.

[14] See Hanzlik, Scott and Thoburn, Arch. Int. Med., 1917, **19**, 1029; Hanzlik, Scott and Reycraft, Ibid., 1917, **20**, 329.

Postmortem Appearances.—The mucous membrane of both stomach and intestines may be hyperemic, or the lesions may be those of a true gastritis or enteritis. There is hyperemia of most of the organs, the lungs often being intensely congested and edematous, and multiple hemorrhages of the heart, lungs, and meninges may be noted, as evidence of the marked changes taking place in the vascular system[1]. The kidneys may show evidences of acute nephritis, while the liver may exhibit fatty changes.

Elimination.—Salicyclic acid circulates in the blood as sodium salicylate, and is found in practically all the organs and secretions of the body. According to Cushny, "About three-fourths of that ingested is excreted by the kidneys, for the most part unchanged, in smaller amount in a combination with glycine, which is known as salicyluric acid . . . It appears in the urine within an hour of its administration by the mouth and is all eliminated in forty-eight hours. It has also been found in the milk, perspiration and bile, but does not appear to be excreted into the stomach nor is any found in the feces. About 20 per cent or more is completely destroyed in the tissues." In the case of methyl salicylate, the urine may contain both the free ester and the combined salicylate, while phenyl salicylate appears in the urine both as salicyluric acid and as the products of oxidation of phenol.

Detection.—Salicylic acid and its salts may be extracted by heating the finely divided tissues with acidified water on the water-bath for some time. Filter, make the filtrate alkaline with sodium carbonate, and evaporate to dryness. Dissolve this residue in dilute sulphuric acid and extract the solution repeatedly with ether[2]. On evaporation of the ether extracts, the salicyclic acid is left behind as a crystalline residue, and may be identified by the following tests.

1. A watery or alcoholic solution of the above residue gives a violet color on the addition of a few drops of dilute ferric chloride solution. Presence of free mineral or of many organic acids, or of free alkalies

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[1] See Wetzel and Nourse, Arch. Path. & Lab. Med., 1926, **1,** 182; Woodbury and Nicholls, Canad. Med. Assoc. Jour., 1928, **18,** 167.

[2] Salicylic acid is easily volatile with steam, so that in the usual systematic process of examination for volatile poisons the salicylic acid will come over and be found in the distillate. This is, probably, the simplest method of detecting the presence of salicylic acid in the tissues, but it does not yield as good results for quantitative work, as does the extraction method.

prevents this reaction. This reaction is not characteristic, as it is given by practically any compound having a free phenolic group, although the color tints are different. Further, salicylic acid gives, also, a red color with Millon's reagent, and a precipitate with bromine-water, as discussed under Phenol.

2. Heat in a test-tube a small amount of the suspected residue with 1 cc. of methyl alcohol and ½ cc. of concentrated sulphuric acid. Allow the mixture to cool, and heat again. In the presence of salicylic acid, the odor of methyl salicylate (wintergreen) is noted.

3. *Jorissen's Test.*—Dissolve some of the residue from the ether extract in 10 cc. of water. Place in a test-tube and allow to cool. Add 4 or 5 drops of 10 per cent. potassium nitrite solution, 4 or 5 drops of 50 per cent. acetic acid, and 1 drop of 10 per cent. cupric sulphate solution. Mix thoroughly, heat to boiling, and continue the boiling for 1 to 2 minutes. In the presence of salicylic acid a blood red color will develop.

Determination.—Thoroughly extract a weighed amount of the finely divided tissue by heating with acidified water on the water-bath for some time. Follow the procedure outlined above, taking special care to extract the acidified solution thoroughly with ether. When the crystalline residue, mixed with more or less fat and other impurities, is obtained, dissolve this residue in about 50 cc. of ether, and transfer this to a separatory funnel. Extract with at least 4 successive portions of 15 cc. each of 1 per cent. ammonium hydroxide. Combine the alkaline aqueous extracts, which contain the salicylic acid as the salt, acidify with dilute hydrochloric acid (1:3), and again extract with ether two or three times. Wash the ether extracts with water until the washings are free from acid (as shown by a yellow color with methyl orange solution). Distill slowly the greater portion of the ether, and allow the remainder to evaporate spontaneously, when the salicylic acid will be left in a very pure form. Dissolve this residue in a small quantity of hot water, and, after cooling, dilute to a definite volume. Should the solution not be clear, filter through a dry filter. Dilute aliquots of the solution with water and treat with a few drops of 0.5 per cent. ferric chloride solution until the maximum color is developed, being careful to avoid an excess of the reagent. Compare the colors developed with this solution with the color obtained when a standard solution (containing 1 mg. of salicylic acid in 50 cc.) is similarly treated, using a colorimeter, and calculate the amount of salicylic acid in the unknown solution. A simple calculation will then yield the amount of the compound present in the original tissue extracted[1].

Detection of Salicylic Acid Esters.—If poisoning by methyl salicylate, phenyl salicylate, or acetylsalicylic acid be suspected, the finely divided tissues should be extracted with warm alcohol, as the first two of these compounds are not readily soluble in acidified water, while the last one mentioned may be easily saponified by heating with an aqueous menstrum. On filtering the alcoholic solution and evaporating carefully, the extracted compound is left behind as a residue, which should be dissolved in ether. On now evaporating the ether the compound will be left as an oil, or as a crystalline residue, depending on which one of the esters is present. It should be remembered that the esters themselves do suffer more or less hydrolysis in the system, so that the products extracted may be in the form of the cleavage products, rather than as the esters themselves, although a certain amount of the original substance ingested will, probably, be obtained, if the extraction processes have been carefully carried out.

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[1] *Official and Tentative Methods of Analysis of the Association of Official Agricultural Chemists*, 2nd ed., 1925, p. 126.

If the product obtained on evaporating the ethereal solution be a liquid, it may be methyl salicylate. This may be recognized by its characteristic odor, and by the violet color obtained on adding a drop of ferric chloride solution to a drop of the suspected liquid dissolved in about 5 cc. of water.

If the product obtained on evaporating the ethereal solution be a solid, it may consist of salicylic acid, phenyl salicylate, acetylsalicylic acid, mixed with traces of phenol. Salicylic acid may be detected by the tests outlined above. Phenyl salicylate may be recognized by the violet color given on addition of ferric chloride to an alcoholic solution, and by the fact that heating a small amount of the residue with a little dilute sodium hydroxide solution and then acidifying with hydrochloric acid, when salicylic acid separates and the odor of phenol is obtained. Should there be enough of the residue, a melting-point determination will show a melting point between 41° and 43°C. If the phenyl salicylate has been completely hydrolyzed in the body, the phenol may be separated from the salicylic acid by dissolving some of the residue in ether, alkalinizing with sodium carbonate solution and shaking, when the phenol remains in the ether, while the salicylic acid passes into the aqueous layer.

If acetylsalicylic acid be suspected, the residue will be easily soluble in cold water, and this solution will not, unless hydrolysis has taken place, give a violet color with ferric chloride solution. If, however, the aqueous solution be heated for a few minutes, a beautiful violet color is obtained on adding ferric chloride solution.. Further, if a little of the residue be boiled with a small amount of dilute sodium hydroxide solution, cooled, and dilute sulphuric acid be added, a white precipitate of salicylic acid forms, and the odor of acetic acid becomes apparent. It should be remembered that acetylsalicylic acid is very easily hydrolyzed, so that, on testing the cold water solution of the residue with ferric chloride, a violet color may obtain, but the test for the presence of both salicylic and acetic acids, after hydrolyzing with sodium hydroxide, will readily identify the product. If enough of the residue remains, a melting point of about 132°C. will yield further confirmatory evidence.

NITROBENZENE

The various nitro substitution products of benzene are all poisonous, the mono-substitution derivative being, probably, the least toxic, although the one leading to the most frequent cases of poisoning. Nitrobenzene is widely employed in the aniline industry and is a very important dye intermediate. It finds some use in the manufacture of explosives, in various dyes for shoes and clothing, as an ingredient in floor polishes, inks, etc., in the preparation of soaps, perfumes, and, formerly, as a flavoring extract in confectionery and liquors. The higher homologues of nitrobenzene seem to decrease in toxicity with increasing molecular weight. The di- and tri-nitro benzene derivatives, however, appear to be somewhat more toxic than mononitrobenzene. These latter derivatives are not only dye intermediates, but find wide application in the manufacture of high explosives, the meta-dinitrobenzene being used in such explosives as roburite and securite. Mononitrobenzene, as found in commerce, is rarely pure, being contaminated, especially, by nitrotoluene and dinitrothiophene.

Mononitrobenzene has caused severe and fatal poisoning on being taken internally, "when used as a substitute for flavoring agents[1] or in alcoholic liquors[2], or in confectionery or pastry", while other cases have arisen from its accidental ingestion, from its use as an abortifacient[3], or as a means of committing suicide[4]. A large number of poisonings are reported from the wearing of shoes or clothing dyed with liquids containing this compound along with aniline, it being difficult in some cases to decide which is the etiologic factor. Up to 1925, there had been reported in the medical literature 47 cases of poisoning from shoe dyes, 25 of which were from nitrobenzene, 21 from aniline, and 1 from an undetermined toxic agent. Of these only 1 was fatal[5], and, strangely enough, all 25 of the nitrobenzene poisonings occurred in the United States, while the 21 aniline cases were in foreign countries. Muehlberger[6] has added to this list 4 nitrobenzene cases, and 6 due to aniline, these latter being the first cases of this type of aniline poisoning reported in the United States[7], other cases being reported later[8]. Similar poisonings have occurred in infants from lying on cloths or diapers marked with inks containing nitrobenzene or aniline[1]. Further, poisoning has occurred from the application of nitrobenzene ointment in the treatment of scabies or as a vermicide (delousing) agent[2]. According to Witthaus[3], "Of 96 reported cases, 69 were accidental, 14 suicidal, 9 to procure abortion, and in 4 the motive was not stated." Industrial poisoning from nitrobenzene occurs from inhalation of the fumes or fine dust, but the most important mode of entrance into the body is through the skin, as a result of spilling the compound on the clothing.[4]

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[1] See Ames, Boston Med. and Surg. Jour., 1907, **156,** 203; and Tuszewski, Ther. der Gegenwart, 1919, **21,** 326.

[2] See Bondi, Prag. med. Wchnschr., 1894, **19,** 129 and 143; Spinner, Pharm. Zentralbl., 1913, **54,** 871; Scott and Hanzlik, Jour. Amer. Med. Assoc., 1920, **74,** 1000; Loeb, Bock, and Fitz, Amer. Jour. Med. Sci., 1921, **161,** 539.

[3] See Schnopfhagen, Wien. klin. Wchnschr., 1927, **40,** 998.

[4] See Litten, Berl, klin. Wchnschr., 1881, **18,** 23; Werner, Ibid., 1884, **21,** 58; Schild, Ibid., 1895, **32,** 187; Paterni, Policlinico, Med. Sec., 1921, **28,** 353.

[5] Stone, Jour. Amer. Med. Assoc., 1904, **43,** 977.

[6] Jour. Amer. Med. Assoc., 1925, **84,** 1897. One of these cases was fatal and was given to Muehlberger by Dr. H. G. Wells of the University of Chicago.

[7] See Young, Muehlberger, and Meek, Jour. Pharm. and Exp. Therap., 1926, **27,** 101.

[8] See Patek, Jour. Amer. Med. Assoc., 1926, **86,** 944; Shinabery, Jour. Indiana Med. Assoc., 1927, **20,** 296; Levin, Jour. Amer. Med. Assoc., 1927, **89,** 2178; Haft, Ibid., 1928, **90,** 742; and Schmitt, Ibid., 1928, **91,** 726.

Properties.—Nitrobenzene ("essence or oil of mirbane", "imitation oil of bitter almonds", $C_6H_5NO_2$) is a pale-yellow, oily liquid, with a sweet taste and an odor very much like that of oil of bitter almonds. According to the International Critical Tables, it has a melting point of 5.7°C., a boiling point of 210.9°C., and a specific gravity of 1.207 at 20°C. It is insoluble in water, but easily soluble in alcohol, ether, glacial acetic acid, etc.

There are three dinitrobenzenes. The ortho compound crystallizes in plates, which melt at 116.5°C., and boil at 319°C. The meta derivative (DNB) forms colorless crystals melting at 89.7°C., while the para substitution product appears as colorless needles melting at 172.1°C. The meta derivative appears to be the most important toxicologically. Hamilton says "By general agreement it is pronounced to be the most troublesome compound that is used in coal-tar manufacture. This does not mean that it is the most toxic of the intermediates, for it is not, but that the requirements of manufacture are such that men are necessarily brought in contact with it in such a way as to make it difficult to protect them." The three trinitrobenzenes have not assumed much importance toxicologically.

Action.—The effects shown by nitrobenzene are due partly to changes in the blood, and partly to action on the central nervous system, the latter being first stimulated and then paralyzed. There is some difference of opinion among investigators as to the action of nitrobenzene on the blood. The blood becomes chocolate-brown in color, and the blood count and hemoglobin fall. Microscopic examination shows that the red cells are altered in size, shape, and staining properties, and, later, signs of regeneration of the cells may be observed in stippled and nucleated red cells. Methemoglobin has been said to be formed early in the poisoning, but spectroscopic examination of the blood often fails to show the characteristic absorption bands. Filehne[1] was not able to show in dogs the formation of methemoglobin, although he found an absorption band between the yellow and red, which did not correspond to any of the ordinary hemoglobin products, and has been called the nitrobenzene-hemoglobin band. In the cases, however, reported by Stifel[2] and by Scott and Hanzlik[3], methemoglobin was observed spectroscopically. Van Slyke and Vollmund[4] state that the reduction in the oxygen capacity of the blood found by them in nitrobenzene poisoning was probably due to the production of anemia and not to the formation of methemoglobin, while Levin[5] was not able to show the production of methemoglobin in the blood of cats, rats, dogs, guinea-pigs, rabbits, or man *in vitro*, while in dogs, cats, and rats this hemoglobin derivative was produced *in vivo*. Likewise, in aniline poisoning in dogs and rabbits by Young, by Muehlberger, and Meek[6], methemoglobin could not be demonstrated spectroscopically. "The blood contains a much smaller amount of oxygen than normally, in some cases only 1 per cent. instead of 17." The oxygen capacity of the blood in human cases has been found reduced, in one case being only 6.2 volumes per cent[7]. Stimson[8] finds that nitrobenzene poisoning in rabbits produces in the circulating blood a non-oxygen-carrying pigment varying in amount from 2.2 to 14.7 per cent. of the total blood pigment, and that this inactive pigment did not give the spectrophotometric picture characteristic of methemoglobin. This decrease in the oxygen-carrying power of the blood leads to the appearance of abnormal products in the urine, para-amidophenol being found both in the blood and urine.

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[1] See Winckel, Deutsch. med. Wchnschr., 1879, **5**, 303, 319, 415, 431, and 447; Rayner, Brit. Med. Jour., 1886, **1**, 294; Ewer, Deutsch. med. Wchnschr., 1920, **46**, 1078; Thomsen, Münch. med. Wchnschr., 1921, **68**, 399; Neuland, Med. Klin., 1921, **17**, 903; Editorial, Jour. Amer. Med. Assoc., 1921, **77**, 1108.

[2] See Linnosset, Union méd., 1874, **28**, 109; Sterne, Rev. méd. de l'est, 1905, **37**, 444; Wolpe, Deutsch. med. Wchnschr., 1920, **46**, 100.

[3] *Toxicology*, 1911, p. 1213.

[4] See Hamilton, *Industrial Poisons in the United States*, 1925, p. 496.

Symptoms.—When taken internally, there is a burning sensation, followed by numbness and tingling, the toxic symptoms often being delayed for varying periods. The face becomes grayish or gray-blue, the lips and nails purple. There is a sense of fulness and throbbing in the head, which may be followed by a violent throbbing headache, nausea and vomiting come on, and dizziness, roaring in the ears, and disturbances of vision are noted. There is a sensation of weakness in the knees, the gait becomes unsteady and staggering, muscular twitchings may occur, these being more often noted in the muscles of the face and jaws. The breath may have a strong odor of oil of bitter almonds. The pulse is weak, rapid and irregular, the respiration is shallow and quick, and, not infrequently, of the Cheyne-Stokes type. The temperature falls, and coma may come on rapidly from failure of the respiration, and collapse and death follow. The urine is dark in color, may smell of nitrobenzene, and may show evidences of renal irritation in the presence of small amounts of albumin, although casts are not commonly found. Methemoglobin has been reported in the urine, but this is probably rare. Hematuria may occur in some cases, Haft[1] reporting gross bleeding from the urinary tract in a case of shoe-dye poisoning, due, possibly, to aniline rather than nitrobenzol. The urine may show reducing properties, but whether or not this is sugar has not been definitely determined. If the patient survives the acute stages, recovery may follow rather rapidly.

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[1] Arch. f. exp. Path. und Pharm., 1878, **9**, 329. See, also, Price-Jones and Boycott, Guy's Hosp. Rep., 1909, **63**, 309.

[2] Jour. Amer. Med. Assoc., 1919, **72**, 395.

[3] Jour. Amer. Med. Assoc., 1920, **74**, 1000.

[4] Jour. Biol. Chem., 1925, **66**, 415.

[5] Jour. Amer. Med. Assoc., 1927, **89**, 2178.

[6] Jour. Pharm. and Exp. Ther., 1926, **27**, 101.

[7] Loeb, Bock, and Fitz, Amer. Jour. Med. Sci., 1921, **161**, 539.

[8] Jour. Biol. Chem., 1927, **75**, 741.

If the poison be absorbed through the skin, as in cases of shoe-dye poisoning, or through the lungs, the symptoms may appear rapidly, collapse coming on within a few minutes and death in an hour, or they may be somewhat delayed. In some of these cases, however, the peculiar blue-gray cyanosis may be the only symptom noted for some time, and, then, suddenly collapse and death occur. In those that are less acute, the train of symptoms above mentioned will obtain.

In the industrial cases in which nitrobenzene is spilled or splashed on the clothing or skin, the symptoms of collapse are, often, manifested very rapidly, as in a case cited by Hamilton[2]. Industrial workers occasionally suffer from a form of chronic poisoning in which languor, somnolence, dyspnea, blueness of the face and lips, and, sometimes, failure of the sight are common symptoms, while multiple neuritis, emaciation, and anemia may be added to the picture in certain cases.

Fatal Dose.—The fatal dose of nitrobenzene is not well-established. In some of the early cases we find such statements as "the bottle was only touched to the lips", the fluid was "merely tasted", and "a little" was taken, all of which are too indefinite for statistical figures. Kobert[3] states that 7 to 8 drops have caused death, Witthaus[4] cites a case in which death was caused by 15 drops, while Gadamer[5] believes that the fatal dose is about 20 drops, and Hunt and Gettler[6] state that "From ½ to 1½ drams (1.85–5.55 cc.) would probably, under ordinary circumstances, cause death; smaller quantities would probably be fatal under some conditions, while recovery would follow much larger doses under appropriate treatment."

Fatal Period.—According to Witthaus[7], "Of 33 fatal cases in which the duration is stated 21 were fatal in 24 hours or less, average 7 hours; 7 in 24 to 48 hours, average 30 hours; and 5 in periods longer than 48 hours." Death has taken place within an hour of spilling nitrobenzene on the clothing[8], and within 3 hours after its ingestion[9].

[1] Jour. Amer. Med. Assoc., 1928, **90**, 742. See, also, Schmitt, Ibid., 1928, **91**, 726.

[2] Jour. Ind. Hyg., 1919, **1**, 200.

[3] *Lehrbuch der Intoxikationen*, 2te. Aufl., 1906, p. 798.

[4] *Toxicology*, 1911, p. 1216.

[5] *Lehrbuch der chemischen Toxikologie*, 2te. Aufl., 1924, p. 345.

[6] "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 723.

[7] *Loc. cit.*, p. 1215.

[8] See Hamilton, *Industrial Poisons in the United States*, 1925, p. 497.

[9] Brennan, Union méd. du Canada, 1887, n. s., **1**, 449.

Treatment.—If the poisoning has occurred from spilling nitrobenzene on the clothing or from its absorption from freshly dyed shoes, etc., the person should be removed from all contact with the poison, by stripping off the clothing, or by removing the shoes, and a warm bath given at once. This may prove all that is necessary, but some of the cases prove fatal even with these precautions. Should signs of collapse occur, bleeding followed by saline infusion, or blood transfusion, are indicated. If the poison has been ingested, the stomach should be promptly washed out with warm water until the return fluid no longer smells of nitrobenzene. A saline purge may, also, be of some value in delaying further absorption of the poison. If respiratory failure appears imminent, inhalation of oxygen should be resorted to at once, and bleeding followed by saline infusion should be adopted for signs of collapse. Such measures are by no means always successful, as, for instance, in Schnopfhagen's case[1] death occurred 3 hours after transfusion of 800 cc. of properly selected blood.

Postmortem Appearances.—The surface of the body may be gray-blue, and the lips are livid, the livores appearing darker than usual. The organs have the odor of bitter almonds, this odor often persisting for some days, while the similar odor found in cases of hydrocyanic acid poisoning, usually, disappears rather quickly. The abdominal viscera, and the brain may be congested. The blood is fluid and usually chocolate colored. In the case of Wells[2], the liver showed a condition resembling that of acute yellow atrophy.

Detection.—The stomach contents or the finely divided tissues should be distilled with steam. The distillate is extracted with ether. On evaporation of the ether, the nitrobenzene is left as a residue, which appears as a yellowish, oily material with the odor of bitter almonds. This residue is then subjected to the following tests.

1. *Morpurgo's Test.*—Place 2 drops of liquid phenol, 3 drops of water, and a piece of potassium hydroxide about the size of a pea in a porcelain dish and heat to boiling. Add a few drops of the suspected liquid and continue the boiling. If nitrobenzene be present, a carmine-red color is produced at the edges of the liquid, which changes to emerald-green on addition of a concentrated solution of calcium hypochlorite.

2. *Reduction to Aniline.*—This is, probably, the most certain method of detecting nitrobenzene. Dissolve a portion of the suspected residue in warm dilute alcohol, add some zinc dust or granulated tin, and treat the mixture with concentrated hydrochloric acid, adding a few drops of this latter reagent at a time, until there is a brisk evolution of hydrogen. After this action has proceeded for about ½ hour, or until the odor of nitrobenzene has disappeared, pour off the acid solution from the zinc or tin, and add an excess of sodium or potassium hydroxide solution. On extracting this alkaline solution with ether, and evaporating the

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[1] Wien. klin. Wchnschr., 1927, **40**, 998.

[2] Cited by Muehlberger, Jour. Amer. Med. Assoc., 1925, **84**, 1992.

ethereal solution, aniline will be left as an oily residue, which may be detected by the tests outlined later under aniline.

ANILINE

Aniline and its derivatives find wide application in various industrial processes, such as manufacture of dyes, use in rubber works, and other chemical procedures. It is, not infrequently, used in printers' ink, in dyes for shoes and clothing, and in the lead of indelible pencils. The crude aniline oil, which is so extensively used in the dye industry, contains, among other impurities, nitrobenzene, mixed toluidines and xylidines, so that the toxic action is not, in all cases at least, due to the presence of pure aniline.

Aniline and its derivatives find access to the body through the skin, lungs, and the stomach, the latter largely by contamination of the hands of the workers with the poison before eating. Probably, the largest number of cases of aniline poisoning are industrial in origin[1], the worker either inhaling the fumes or absorbing the aniline through the skin. "Of 128 cases of industrial poisoning reported in a German dye factory, 109 were due to aniline."[2] Many cases are reported in rubber works[3], where aniline is used in different processes, from its use as a wash for printers' ink[4], and among dyers and painters[5]. Poisoning from either nitrobenzene or aniline has been often reported, the toxic effects arising from wearing of shoes dyed with aniline-containing liquids, about 68 such cases being found in the literature[6], while a few cases have arisen in infants through absorption of aniline from diapers marked with aniline dyes. Although aniline poisoning is by no means uncommon, relatively few fatalities have occurred, Hamilton mentioning 3 industrial cases, and Stone[7] reporting one death from shoe dye.

Properties.—Aniline (amidobenzene, $C_6H_5NH_2$) is a colorless or nearly colorless, highly refractive, oily liquid with a characteristic odor and a burning taste. It has a specific gravity of 1.022 at 20°C. and boils at 184.4°C. It is soluble in 31 parts of water, and is miscible in all proportions with alcohol, ether, benzene, chloroform, carbon disulphide, and fixed or volatile oils. Although feebly basic, it is without action on litmus paper. In aqueous solution, the aniline salts usually show an acid reaction.

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[1] See Newton, Jour. Amer. Med. Assoc., 1920, **74**, 1149.

[2] Hunt and Gettler, "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 729.

[3] See Luce and Hamilton, Jour. Amer. Med. Assoc., 1916, **66**, 1441; Cronin, Boston Med. and Surg. Jour., 1924, **191**, 683; and Hamilton, *Industrial Poisons in the United States*, 1925, p. 502.

[4] Apfelbach reported in 1913 the earliest poisoning from aniline in American literature, which arose from this source (cited by Hamilton, *Loc. cit.*)

[5] See Birge, Jour. Amer. Med. Assoc., 1914, **62**, 314.

[6] For a discussion of this phase see page 815.

[7] Jour. Amer. Med. Assoc., 1904, **43**, 977. See, also, Müller, Deutsch. med. Wchnschr., 1887, **13**, 27; and Smith, Lancet, 1894, **1**, 89.

Symptoms.—The action of aniline is quite similar to that of nitrobenzene in that it first stimulates and later paralyzes parts of the central nervous system, but its most characteristic effects are exerted upon the blood. The most marked symptom in aniline poisoning is the grayish-blue color of the finger nails, the face, lips, tongue, and mouth. Workers in the aniline industry are so prone to show this cyanosis that they are quite commonly called "blue boys". This coloration has been supposed to be due to the formation of methemoglobin, and this pigment has been reported as found spectroscopically in some cases, but, according to the work of Young, Muehlberger and Meek[1], the brownish coloration of the blood is due to paramino-phenol and not to methemoglobin, their clinical observations being supported by their failure to produce methemoglobin in experimental animals. The later blood changes are a diminution in the amount of hemoglobin, and the appearance of stippled red cells and cells of variable size and shape. Along with this cyanosis the acute cases usually show headache, dizziness, weakness, staggering gait, nausea and, occasionally, vomiting, dryness of the throat, labored speech, slow respirations, a weak, rapid, feeble, often dicrotic, pulse, with a fall in blood pressure. Electrocardiographic tracings seem to show that aniline exerts a direct toxic action on the heart muscle, as well as on the specialized conductive tissue, so that all types of arrhythmia and, even, heart block may occur. In the more severe cases, the headache may become intense, the patient becomes drowsy, convulsions may occur, and coma, rarely followed by death, may obtain. Usually, a case of aniline poisoning may not incapacitate a person for more than several days, although complete recovery may not occur for 5 or 6 weeks.

In the chronic cases, there may be headache, digestive disturbances, skin eruptions, anemia, various nervous symptoms in both sensory and motorareas, muscular weakness, and palpitation of the heart on exertion. The cyanosis is marked and may, when associated with the above symptoms, lead to the assumption of valvular heart disease, as stated by Hamilton. In the cases studied by Davis[2], some of the men seemed "to acquire a tolerance for aniline, in that they remain cyanotic for years without the development of any apparent serious symptoms. These patients have some blood changes, of course, yet they feel no ill effects except for a slight tired feeling at the end of the day's work." Some of the workers, who have been exposed to aniline for some time, may show symptoms of bladder tumor which may be benign or, sometimes, malignant. These cases begin with hematuria, so that this symptom should excite suspicion. It should be mentioned that in some cases of acute aniline poisoning, hematuria may be present to quite a marked degree, as is shown in the cases of shoe-dye poisoning reported by Haft[1] and by Schmitt[2].

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[1] Jour. Pharm. and Exp. Therap., 1926, **27**, 101. See, also, Levin, Jour. Amer. Med. Assoc., 1927, **89**, 2178.

[2] Jour. Ind. Hyg., 1921–22, **3**, 53.

The urine in both acute and chronic poisoning may be dark in color, and may show no pathologic findings. Paraminophenol is, usually, present in the form of an ethereal sulphate, while in some cases free aniline may be found[3]. While hemoglobin and red blood cells may be occasionally found, yet it would seem that methemoglobin is not frequently present, although it has been reported.

Fatal Dose and Period.—The lethal dose of aniline is uncertain. It would seem to be less than 25 grams as that amount has proven fatal to a healthy man,[4] while 25 cc. of aniline oil caused the death of a young woman[5] in 24 hours. In Smith's case[6] death occurred in 12 hours after taking 90 cc. of marking ink consisting largely of aniline. Recovery is said to have followed the taking of 75 cc.[7] In Stone's fatal case[8] of shoe-dye poisoning, the amount absorbed is, of course, not known.

Treatment.—If the aniline has been taken by mouth, gastric lavage should be instituted at once, and this should be followed by saline purgatives and such stimulants as hot coffee and strychnine. If the patient has been affected in an industrial plant, he should be quickly removed into the fresh air and any aniline-soaked clothing removed. Young, Muehlberger and Meek[9] believe that cardiac and not respiratory treatment is indicated in aniline poisoning, especially in the acute stage. In the serious cases, bleeding followed by saline infusions or blood transfusions is indicated. Oxygen inhalations may prove of value. Under all circumstances the patient should be kept warm.

Postmortem Appearances.—The autopsy findings show little that is characteristic. In some cases, the appearances may resemble those discussed under pyrogallol. The blood is chocolate colored and shows the presence of paramino-phenol. The odor of aniline may be noticed in most of the organs.

Detection.—Aniline is only feebly basic, so that it will pass over with steam, to some extent, from an acidified solution. It is preferable, however, to make the aqueous suspension of the tissues strongly alkaline and distill with steam. If the quantity of aniline is large, oil droplets may appear in the aqueous distillate, but, in many cases, the aniline remains in solution in the water. Shake out the distillate with ether, remove the ether layer and allow it to evaporate, when brownish drops of aniline remain in the residue. This residue should be examined for the characteristic odor and the following tests applied.

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[1] Jour. Amer. Med. Assoc., 1928, **90**, 742.

[2] Ibid., 1928, **91**, 726.

[3] See Möllerström, Acta. Med. Scand., 1929, **71**, 73.

[4] See Kobert, *Lehrbuch der Intoxikationen*, 2te. Aufl., 1906, **2**, 789, and Autenrieth, *Detection of Poisons*, 6th Amer. Ed., translated by Warren, 1928, p. 71.

[5] Müller, Deutsch. med. Wchnschr., 1887, **13**, 27.

[6] Lancet, 1894, **1**, 89.

[7] Hunt and Gettler, "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 730.

[8] Jour. Amer. Med. Assoc., 1904, **43**, 977.

[9] Jour. Pharm. and Exp. Therap., 1926, **27**, 101.

1. *Hypochlorite Test.*—Dissolve a little of the residue in water and add a few drops of calcium or sodium hypochlorite solution, avoiding an excess, when a reddish-violet to a violet-blue color will appear, which gradually changes into a dirty red, if aniline be present. Addition of a little dilute ammoniacal solution of phenol to this violet or dirty red solution will produce a pure blue color. This latter modification (the indophenol reaction) is sensitive to 1 part in 66,000.

2. *Phenyl-isocyanide Test.*—Dissolve a little of the residue in water and add a few drops of chloroform and a little potassium hydroxide solution. On heating this mixture the disagreeable odor of phenylisocyanide will be noticed, if aniline be present.

3. *Chromic Acid Test.*—Place in a small porcelain capsule or spot plate a little of the suspected residue. Add one or two drops of concentrated sulphuric acid and draw through this solution several times a small crystal of potassium bichromate. A greenish color is first observed, which slowly changes into a blue shade. Addition of 1 or 2 drops of water will produce at once a pure blue color, but in the presence of much water the color may be greenish or even black. This reaction must not be confused with that produced by these reagents with strychnine, as the color with strychnine passes through various shades of purple, to red, while the reaction with aniline remains blue for some time and finally disappears. Of course, strychnine would not be found in the distillate, so that no question should be raised as to this possibility, but, occasionally, a witness is asked as to such a condition of affairs.

4. If a little of the residue be dissolved in water and treated with bromine water, a flesh-colored precipitate of tribromaniline will appear; if aniline be present in concentration of 1 part in 69,000, according to Landolt. This compound may be distinguished from tribromphenol by the fact that it melts at 118°C., while tribromphenol has a melting point of 96°C.

ACETANILID

Acetanilid has been known in chemistry for some time and was introduced by Cahn and Hepp in 1886 as an analgesic and antipyretic under the name of *antifebrin.* Poisoning from acetanilid is, largely, accidental, resulting from overdoses of the drug for the relief of headache, although a few cases of attempted suicide have been reported. In combination with caffeine, acetanilid has been employed in various headache remedies, among which are "Antikamnia", "Bromo-Seltzer", "Orangeine", "Koehler's Headache Powders", etc. These compounds have lead to many serious cases of poisoning[1], both acute and chronic, and are accountable, to a very large extent, for the rather widespread "acetanilid habit". Although acetanilid is quite toxic, there is little restriction placed on the sale of these proprietary preparations, so that the public may readily obtain them. According to Kebler, Morgan, and Rupp[1], of 614 cases of poisoning reported by physicians to the U. S. Department of Agriculture, 325 cases arose from the use of acetanilid without a physician's prescription. Other cases of poisoning have arisen from the external application of acetanilid to burns, wounds, and other inflammatory conditions of the skin[2]. It is probable that many cases of chronic acetanilid poisoning occur that may escape recognition, and are not reported in the literature. Hunt and Gettler state that 10.7 per cent. of recorded cases are of this type.

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[1] See, for instance, Hemenway, Jour. Amer. Med. Assoc., 1906, **47**, 2158; Smedley, Ibid., 1907, **48**, 1433; Wynn, Ibid., 1907, **49**, 1027.

Properties.—Acetanilid (Monoacetyl aniline, "antifebrin", C_6H_5-$NHCH_3CO$) occurs as colorless, shining, crystalline leaflets, or a white, crystalline powder, possessing a slightly burning taste, and having no odor. It is soluble in 190 parts of water, 3.4 parts of alcohol, 3.7 parts of chloroform, 17 parts of ether, 4 parts of acetone, 47 parts of benzene, and about 5 parts of glycerin, at 25°C.; in 20 parts of boiling water, and in 0.6 part of boiling alcohol. It melts at 114.2°C.

Symptoms.—The effects of acetanilid vary with the dose and with the individual. "Many persons can take very large doses without apparent effect, while in others comparatively minute quantities produce symptoms of greater or less importance." In mild cases the chief symptom is a somewhat marked cyanosis which is especially marked under the finger nails, and on the lips and extremities. In the severe acute cases this cyanosis is intense and long-continued. It has been supposed to be due to the formation of methemoglobin, but recent work of Young and Wilson[3] would seem to cast some doubt on this generally accepted statement since these workers were unable to show the formation of methemoglobin in their experimental animals. As paraminophenol is produced in the system following both aniline and acetanilid poisoning, it would seem probable that the cyanosis may be traceable to this substance rather than to methemoglobin. Following the cyanosis, great weakness, prostration and collapse, with coldness of the extremities, profuse sweating, feeble, rapid pulse, weak, shallow respiration and unconsciousness may be noted. In some cases there may be marked restlessness, convulsions, and delirium, although the cerebral symptoms are more often dulness, confusion, and coma. The temperature may be subnormal, and the pupils slightly dilated. If the case progresses for a few days, there is a progressive destruction of the red cells, the blood picture resembling closely that seen in pernicious anemia, although there may be an associated leukocytosis. This destruction of the red cells may be associated with an acute nephritis, and an acute progressible jaundice may be noted[1]. Death is due, according to Young and Wilson, to cardiac weakness, rather than to respiratory failure.

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[1] Bull. 126, Bureau of Chemistry, 1909.

[2] "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 736. See, also, Stewart, Jour. Amer. Med. Assoc., 1905, **44**, 1725; Austin and Larrabee, Ibid., 1906, **46**, 1680; Blackburn, Ibid., 1767; Gordinier, Boston Med. and Surg. Jour., 1911, **165**, 198; McEllroy, Jour. Amer. Med. Assoc., 1919, **73**, 1927.

[3] Jour. Pharm. and Exp. Therap., 1926, **27**, 133.

In the chronic cases the symptoms consist of disturbances of digestion, general weakness, cyanosis, tremor, general mental debility or nervous excitability, insomnia and dyspnea on exertion. The blood is often chocolate colored, thought to be due to methemoglobin, although, in part at least, rather to paraminophenol, and shows a blood picture resembling that of pernicious anemia. The fall in the red cell count, percentage of hemoglobin, and oxygen capacity appears to be parallel. The urine is dark in color, may contain blood pigments, methemoglobin having been reported in some cases, and gives the indophenol reaction. If the poisoning be intense and continued, gradually increasing weakness, emaciation, weakness, collapse, and death occur.

Fatal Dose and Period.—In those especially susceptible or weakened by disease, especially those suffering from weak hearts, severe and even fatal results may be observed after doses of 5 to 10 grains. Thomas[2] attributes death of a febrile patient to 5 grains, Smedley[3] reports death following the intake of 7.5 grains, while Sanford and Van Wagman[4] cite the death of a boy of seven 2 hours after ingestion of the third dose of 4.5 grains. Recovery has followed, however, the intake of such large doses as 28 grams (432 grains)[5]. Death may be rather sudden (a few hours) or be delayed for several days.

Treatment.—The treatment is practically the same as that discussed under aniline, special attention being paid to the cardiac symptoms. In the chronic cases, the treatment consists of prompt withdrawal of the drug and giving attention to the symptoms as they arise.

Postmortem Appearances.—These are not characteristic. The blood is, usually, chocolate colored, as in aniline poisoning. In some cases there may be evidences of nephritis and hepatitis.

Detection.—The finely hashed tissue is extracted with 95 per cent. alcohol for several hours. Filter, evaporate the alcohol, and take up the residue with water acidified with sulphuric acid. Shake out this acid solution with ether or chloroform. Evaporate off the solvent and apply the following tests to the residue.

1. *Indophenol Test.*—This test is given by compounds containing a free, primary, aromatic amino group, and has been discussed under aniline. Acetanilid, having no free amino group, must first be hydrolyzed. Take a small amount of the suspected residue and boil with

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[1] See Brown, Amer. Jour. Med. Sci., 1901, **122**, 770.

[2] Indiana Med. Jour., 1890, **9**, 67.

[3] Jour. Amer. Med. Assoc., 1907, **48**, 1433.

[4] Jour. Amer. Med. Assoc., 1907, **48**, 1693.

[5] See Kobert, *Lehrbuch der Intoxikationen*, 2te. Aufl., 1906, **2**, 795.

about 1 cc. of concentrated hydrochloric acid. Cool and add 1 or 2 cc. of a saturated aqueous phenol solution. On now adding, drop by drop, a freshly prepared aqueous solution of calcium hypochlorite and shaking, a more or less intense dirty-red color will be obtained. If ammonia be now added, the mixture will change to a beautiful indigo-blue color. Phenacetine, also, gives this reaction after being hydrolyzed.

2. Boil a little of the suspected residue with a few cc. of alcoholic or aqueous potassium hydroxide solution, when the odor of aniline may be noticeable. Add a few drops of chloroform to the cool solution, and heat again. The disagreeable, offensive odor of phenylisocyanide will be apparent at once. This test is given by aniline itself, but not by phenacetin or other derivatives of para-phenetidin.

3. Heat in a boiling water-bath a rather large portion of the suspected residue with concentrated sulphuric acid and a little alcohol. If acetanilid be present, the characteristic odor of ethyl acetate will appear when a little water is added. This test shows the presence of the acetyl group in the compound and is of special value in identifying the residue.

Acetanilid, as such, does not appear in the urine except when very large doses have been taken. Aceto-para-aminophenol or para-aminophenol are, however, found in conjugation with both sulphuric and glycuronic acids. If a relatively large amount (100 to 500 cc.) of urine be boiled with about 10 cc. of hydrochloric acid under a reflux condenser for an hour or two, para-aminophenol is liberated and may be detected by the indophenol test applied directly to the acidified boiled urine. Should this test prove uncertain, add an excess of sodium carbonate to the cooled boiled urine, and extract several times with large amounts of ether. On drawing off the ether layer and evaporating it, para-aminophenol is left behind as a brownish oily residue. An aqueous solution of this residue will, then, give the indophenol reaction.

ACETPHENETIDIN

Acetphenetidin differs from acetanilid only in the fact that the hydrogen in the para position of the latter is replaced by an ethoxyl group in the former. It is much less dangerous and less toxic than acetanilid, although quite a few cases have been reported. "Of 70 cases recorded in medical literature, 3 (4.2 per cent.) ended fatally; of 95 cases of poisoning collected by the Department of Agriculture, 7 (7.3 per cent.) died."[1] The cases are mostly acute, although chronic ones have been reported[2].

Properties.—Acetphenetidin (monoacetyl para-amidophenetol, "phenacetin", $C_6H_4OC_2H_5.NH.CH_3CO$ 1:4) appears in the form of white, glistening, crystalline scales, or as a fine white, crystalline powder, having a slightly bitter taste and being without odor. It is soluble in 1310 parts of water, 15 parts of alcohol, 14 parts of chloroform, and in about 130 parts of ether at 25°C., while it is soluble in 82 parts of boiling water and 2.8 parts of boiling alcohol. It melts at 135°C.

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[1] Hunt and Gettler, "Non-alkaloidal Organic Poisons" in *Legal Medicine and Toxicology* by Peterson, Haines and Webster, 1923, **2**, 738.

[2] See Hirschfeld, Deutsch. med. Wchnschr., 1905, **31**, 66.

Symptoms.—These are practically the same as those discussed under acetanilid, although they appear somewhat more slowly. The cyanosis is somewhat rare with small doses of phenacetin, although it may be present after larger doses, but is not so marked as with acetanilid. On the other hand, skin eruptions are more prone to occur in phenacetin poisoning[1]. "Among these are skin eruptions of various forms, such as red, erythematous, itching patches or more widely diffused hyperemia resembling the onset of measles or scarlatina; urticaria occurs not uncommonly, while eczema and bullae are rarer. In some cases edematous swelling has been observed."[2]

Fatal Dose and Period.—This can not be definitely stated, as some preexisting disease was usually present in the fatal cases which may have contributed to the fatal result. According to Hunt and Gettler, 6 grains taken within 2 hours are said to have caused the death of a woman of seventy-six, while 10 and 15 grains are also said to have proven fatal. Death may occur, as with acetanilid, rapidly, or be delayed for several days.

Treatment.—The same as discussed under acetanilid and aniline.

Postmortem Appearances.—There is nothing characteristic. The findings are practically the same as shown by acetanilid.

Detection.—Phenacetin is extracted from the tissues by the method given under acetanilid. The residue obtained does not give the phenylisocyanide test, but responds to the indophenol test given under acetanilid. Further tests may be applied as follows.

1. *Oxidation Test.*—Boil a little of the suspected residue for several minutes with a little concentrated hydrochloric acid. Dilute with water and filter when cold. Add to the filtrate a few drops of 3 per cent. chromic acid solution or a drop or two of 8 per cent. potassium dichromate solution, when a ruby-red color appears in the presence of phenacetine. In this test acetanilid gives a yellow color gradually turning to green.

2. *Azo-dye Test.*—Boil a little of the suspected residue with concentrated hydrochloric acid. Dilute with a few cc. of water, cool in ice, add a few drops of 10 per cent. sodium nitrite solution, alkalinize with sodium hydroxide solution, and add a few drops of an alkaline solution of β-naphthol. A red color will appear and change to a dark cherry-red upon the addition of hydrochloric acid. This reaction is given both by acetanilid and phenacetin, and can be obtained with the urine in cases of poisoning from either substance.

3. *Nitration Test.*—Heat some of the suspected residue with 10 per cent. nitric acid, when the phenacetin dissolves with a yellow to orange-red color. If the solution be somewhat concentrated, long yellow needles of mononitrophenacetin (the nitro group being in the ortho

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[1] See Valentin, Therap. Monatsh., 1888, **2**, 330; and West, Lancet, 1895, **1**, 91.

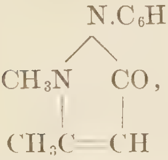
[2] Cushny, *Pharmacology and Therapeutics*, 9th ed., revised by Edmunds and Gunn, 1928, p. 509.

position to the acetyl group) will separate on cooling. These needles melt at 103°C. and are characteristic of phenacetin. Acetanilid gives a colorless solution when heated with dilute nitric acid.

Phenacetin, as such, does not appear in the urine except after intake of rather large doses. Under ordinary circumstances it is hydrolyzed in the system to paraphenetidin and para-aminophenol, both of which compounds are excreted in the form of conjugated glycuronates and sulphates. These compounds may be detected in the urine by the azo-dye test mentioned above and by the indophenol test discussed under acetanilid.

ANTIPYRINE

Antipyrine was introduced as an antipyretic in 1884. "Between that date and 1909," state Hunt and Gettler, "488 cases of poisoning, with 10 deaths, were reported." Most of these cases were medicinal, although it was used for murder in one case[1]. Antipyrine seems to be less toxic than acetanilid, and more poisonous than phenacetin.

Properties.—Antipyrine (phenazone, 1-phenyl-2-3-dimethyl-5-pyrazolon,  $\begin{array}{ccc} & \mathrm{N.C_6H_5} & \\ & / \quad \backslash & \\ \mathrm{CH_3N} & & \mathrm{CO} \\ | & & | \\ \mathrm{CH_3C} & = & \mathrm{CH} \end{array}$, $C_{11}H_{12}N_2O$) occurs as colorless crystals, or as a white, crystalline powder, with a slightly bitter taste and without odor. It is soluble in less than 1 part of water, in 1.3 parts of alcohol, 1 part of chloroform, and in 43 parts of ether at 25°C. It melts between 111° and 113°C.

Symptoms.—The symptoms of poisoning by antipyrine are similar to those of acetanilid, although cyanosis is much rarer[2]. The skin eruptions mentioned under acetphenetidin are, probably, much more common with antipyrine than with the other antipyretics. There may be some irritation of the throat, leading to burning and swelling of the throat and mouth, and, occasionally, nausea and vomiting, which symptoms are not reported with acetanilid or acetphenetidin. The general symptoms of antipyrine poisoning are those previously discussed.

In the chronic form of poisoning, the skin eruptions are especially prominent, while disturbances of digestion, drowsiness and muscular weakness are also observed. Lewin[3] calls attention to a hypersensitiveness which may develop and continue for some time.

Fatal Dose and Period.—Severe symptoms have been observed following doses of 5, 10, and 15 grains. Death has resulted, within a short time, from the administration of 22 grains to a consumptive, while 15 grains have caused death in individuals suffering from angina pectoris. In the Fulham murder case, the dose was 4 drams.

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[1] Fulham Murder Case, Pharm. Jour. and Pharmacist, 1913, **90**, 325.

[2] See Hayes, Brit. Med. Jour., 1896, **1**, 269; and Eisenmann, Therap. Monatsh., 1897, **11**, 233 for cases with cyanosis.

[3] *Nebenwirkungen der Arzneimittel*, 1899, p. 459.

Treatment.—This is the same as that outlined under acetanilid.

Postmortem Appearances.—There is nothing characteristic in the autopsy findings.

Detection.—Antipyrine is rapidly absorbed and rapidly distributes itself in the various organs of the body. It is partially eliminated, as such, in the urine, and partly as a conjugated sulphuric or glycuronic acid. It is readily isolated from the organs by the usual methods of extraction of the alkaloids. While the acid solution obtained in this process may yield certain amounts of antipyrine to both ether and chloroform, much more is obtained from the alkalinized solution, chloroform being a better solvent for it than ether. If the chloroform be evaporated, antipyrin remains as a crystalline residue which may be used for the following tests. Antipyrine gives precipitates with many of the alkaloidal precipitants, especially with tannic acid, picric acid, and potassium-bismuth iodide.

1. *Ferric Chloride Test.*—Dissolve a little of the suspected residue in water and add 1 or 2 drops of a 10 per cent. solution of ferric chloride. A deep red color will be produced if antipyrine is present. Addition of a few drops of dilute sulphuric acid changes the red to a light yellow color.

2. *Nitroso-antipyrine Test.*—Dissolve a little of the suspected residue in water and add a few drops of a dilute solution of potassium nitrite, following this with a little sulphuric acid. In the presence of antipyrine a green color appears. If the antipyrine solution be concentrated, green crystals of nitrosoantipyrine separate on allowing the mixture to stand for some time.

The urine in cases of antipyrine poisoning may have a deep yellow to blood-red color, and, in some cases appears red in transmitted light and green in reflected light. Occasionally, antipyrine may be detected in the urine by the direct ferric chloride test mentioned above. To differentiate this color from that which might be due to other substances, such as diacetic acid for instance, alkalinize the urine and extract with chloroform. Filter the chloroform layer and allow it to evaporate, when the residue may be tested with the tests given above.

CAMPHOR

Camphor is a stearoptene derived from *Cinnamomum Camphora.* It differs from the terpenes in possessing a ketone linking in its molecule. It is employed medicinally as a mild irritant and antiseptic, a counter-irritant, and a stimulant. It has caused poisoning, especially among children, by being mistaken or administered for something else, or by being given in overdose, and has lead to somewhat mild poisoning through its use as a household remedy for colds. It is not infrequently employed as an abortifacient and has caused death when used as such an agent. Witthaus states, "We have seen the reports of 78 cases, of which 60 were 'accidental', 5 suicidal, 8 to provoke abortion, and in 5 the motive is not stated. In twelve cases the poisoning was fatal."[1]

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[1] *Toxicology,* 1911, p. 1088.

Properties.—Camphor ($C_9H_{16}CO$) occurs as white, translucent, tough masses or granules. It has a penetrating, characteristic odor, and a pungent, aromatic taste. It slowly volatilizes at ordinary temperatures. It is soluble in about 800 parts of water, 1 part of alcohol, 0.5 part of chloroform, and 1 part of ether at 25°C., and is freely soluble in carbon disulphide, petroleum benzin, and in fixed or volatile oils. It melts between 174° and 177°C.

Symptoms.—When taken internally camphor acts as an irritant, causing a burning sensation in the throat and stomach, there may be nausea and vomiting from the irritant action on the stomach, and there is some dizziness, headache, with blurred vision, and roaring in the ears. In a variable period, ranging from a few minutes to some hours, there develops a condition much resembling alcoholic intoxication, which may be shown in excitement, hilarity, incoherent talking, delirium, hallucinations, restlessness, and sudden violent movements. There may be mild or severe convulsive attacks, alternating with periods of quiet or, even, unconsciousness, and complete stupor and death may follow. In some cases, there is no period of excitement, unconsciousness coming on suddenly. In some cases there may be symptoms of nephritis, as shown by strangury, albuminuria, or anuria. The face is flushed at first, but later becomes pale, the pupils are dilated, and the conjunctivae may be injected. The pulse may be irregular, and the respiration is little affected except during the convulsions, when it may be markedly slowed. The breath and urine smell of camphor.

Fatal Dose and Period.—Finley[1] reports the death of a child of two years four hours after swallowing about 15 grains, while Davies[2] records the death of a child of two years and eight months, 18 hours after ingestion tion of about 30 grains. The fatal dose for an adult is uncertain, recovery having occurred from about 200 grains[3].

Treatment.—The stomach should be promptly washed out, and saline purgatives or calomel should be used to remove the material from the bowels. The body should be kept warm. The convulsions should be controlled by bromides, or morphine by mouth, while chloral hydrate may be given *per rectum.*

Postmortem Appearances.—There is nothing characteristic in the autopsy findings, beyond the fact that the organs have the odor of camphor. There may be hyperemia and other evidences of gastric irritation, although these are not always present.

Detection.—Camphor distills readily with steam. Shake out the distillate with benzene, separate the benzene layer, and evaporate on a water-bath. The camphor remains as a crystalline residue, which may be identified by its physical properties.

[1] Med. Record, 1887, **31**, 125.

[2] Brit. Med. Jour., 1887, **1**, 726.

[3] Menzies, Edinb. Med. Jour., 1873, **18**, 1004.

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